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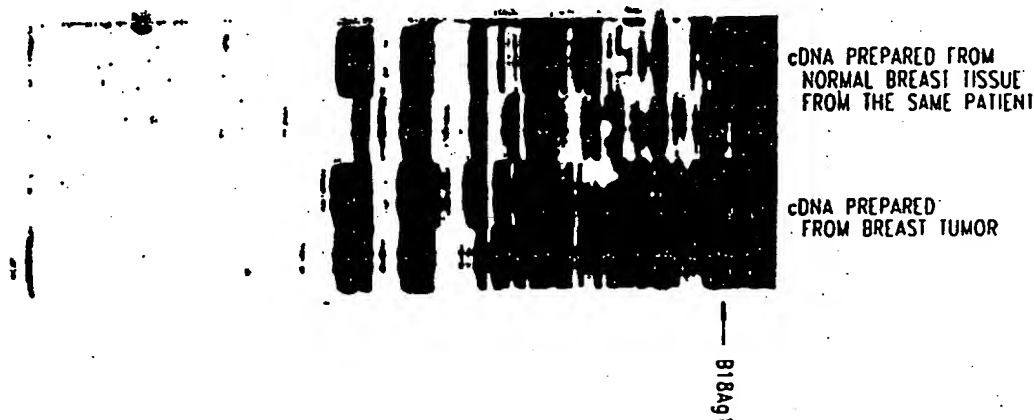
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(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER



(57) Abstract

Compositions and methods for the detection and therapy of breast cancer are disclosed. The compounds provided include nucleotide sequences that are preferentially expressed in breast tumor tissue, as well as polypeptides encoded by such nucleotide sequences. Vaccines and pharmaceutical compositions comprising such compounds are also provided and may be used, for example, for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of antibodies, which are useful for diagnosing and monitoring the progression of breast cancer in a patient.

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COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER

TECHNICAL FIELD

The present invention relates generally to the detection and therapy of breast cancer. The invention is more specifically related to nucleotide sequences that are preferentially expressed in breast tumor tissue and to polypeptides encoded by such nucleotide sequences. The nucleotide sequences and polypeptides may be used in vaccines and pharmaceutical compositions for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of compounds, such as antibodies, useful for diagnosing and monitoring the progression of breast cancer in a patient.

BACKGROUND OF THE INVENTION

Breast cancer is a significant health problem for women in the United States and throughout the world. Although advances have been made in detection and treatment of the disease, breast cancer remains the second leading cause of cancer-related deaths in women, affecting more than 180,000 women in the United States each year. For women in North America, the life-time odds of getting breast cancer are now one in eight.

No vaccine or other universally successful method for the prevention or treatment of breast cancer is currently available. Management of the disease currently relies on a combination of early diagnosis (through routine breast screening procedures) and aggressive treatment, which may include one or more of a variety of treatments such as surgery, radiotherapy, chemotherapy and hormone therapy. The course of treatment for a particular breast cancer is often selected based on a variety of prognostic parameters, including an analysis of specific tumor markers. See, e.g., Porter-Jordan and Lippman, *Breast Cancer* 8:73-100 (1994). However, the use of established markers often leads to a result that is difficult to interpret, and the high mortality observed in

breast cancer patients indicates that improvements are needed in the treatment, diagnosis and prevention of the disease.

Accordingly, there is a need in the art for improved methods for therapy and diagnosis of breast cancer. The present invention fulfills these needs and further provides other related advantages:

SUMMARY OF THE INVENTION

Briefly stated, the subject invention provides compositions and methods for the diagnosis and therapy of breast cancer. In one aspect, isolated polynucleotides are provided, comprising (a) a nucleotide sequence preferentially expressed in breast cancer tissue, relative to normal tissue; (b) a variant of such a sequence, as defined below; or (c) a nucleotide sequence encoding an epitope of a polypeptide encoded by at least one of the above sequences. In one embodiment, the isolated polynucleotide comprises a human endogenous retroviral sequence recited in SEQ ID NO: 1. In other embodiments, the isolated polynucleotide comprises a sequence recited in any one of SEQ ID NO: 3-15 26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

In related embodiments, the isolated polynucleotide encodes an epitope of 20 a polypeptide, wherein the polypeptide is encoded by a nucleotide sequence that: (a) hybridizes to a sequence recited in any one of SEQ ID NO: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under stringent 25 conditions; and (b) is at least 80% identical to a sequence recited in any one of SEQ ID NO: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

In another embodiment, the present invention provides an isolated polynucleotide encoding an epitope of a polypeptide, the polypeptide being encoded by: (a) a nucleotide sequence transcribed from the sequence of SEQ ID NO: 141; or (b) a variant of said nucleotide sequence that contains one or more nucleotide substitutions, deletions, insertions and/or modifications at no more than 20% of the nucleotide positions, such that the antigenic and/or immunogenic properties of the polypeptide encoded by the nucleotide sequence are retained. Isolated DNA and RNA molecules comprising a nucleotide sequence complementary to a polynucleotide as described above are also provided.

10 In related aspects, the present invention provides recombinant expression vectors comprising a polynucleotide as described above and host cells transformed or transfected with such expression vectors.

In further aspects, polypeptides comprising an amino acid sequence encoded by a polynucleotide as described above, and monoclonal antibodies that bind to such polypeptides are provided. In certain embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of SEQ ID NO: 299, 300, 304-306, 308 and 315, and variants thereof as defined below.

In yet another aspect, methods are provided for determining the presence of breast cancer in a patient. In one embodiment, the method comprises detecting, within a biological sample, a polypeptide as described above. In another embodiment, the method comprises detecting, within a biological sample, an RNA molecule encoding a polypeptide as described above. In yet another embodiment, the method comprises (a) intradermally injecting a patient with a polypeptide as described above; and (b) detecting an immune response on the patient's skin and therefrom detecting the presence of breast cancer in the patient. In further embodiments, the present invention provides methods for determining the presence of breast cancer in a patient as described above wherein the polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In a related aspect, diagnostic kits useful in the determination of breast cancer are provided. The diagnostic kits generally comprise either one or more monoclonal antibodies as described above, or one or more monoclonal antibodies that bind to a polypeptide encoded by a nucleotide sequence selected from the group consisting of sequences provided in SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242 and 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and a detection reagent.

Diagnostic kits are also provided that comprise a first polymerase chain reaction primer and a second polymerase chain reaction primer, at least one of the primers being specific for a polynucleotide described herein. In one embodiment, at least one of the primers comprises at least about 10 contiguous nucleotides of a polynucleotide as described above, or a polynucleotide encoding a polypeptide encoded by a sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289 and 290.

Within another related aspect, the diagnostic kit comprises at least one oligonucleotide probe, the probe being specific for a polynucleotide described herein. In one embodiment, the probe comprises at least about 15 contiguous nucleotides of a polynucleotide as described above, or a polynucleotide selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289 and 290.

In another related aspect, the present invention provides methods for monitoring the progression of breast cancer in a patient. In one embodiment, the method comprises: (a) detecting an amount, in a biological sample, of a polypeptide as described above at a first point in time; (b) repeating step (a) at a subsequent point in time; and (c) comparing the amounts of polypeptide detected in steps (a) and (b), and therefrom monitoring the progression of breast cancer in the patient. In another embodiment, the method comprises (a) detecting an amount, within a biological sample, of an RNA molecule encoding a polypeptide as described above at a first point in time; (b) repeating

step (a) at a subsequent point in time; and (c) comparing the amounts of RNA molecules detected in steps (a) and (b), and therefrom monitoring the progression of breast cancer in the patient. In yet other embodiments, the present invention provides methods for monitoring the progression of breast cancer in a patient as described above wherein the polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In still other aspects, pharmaceutical compositions, which comprise a polypeptide as described above in combination with a physiologically acceptable carrier, and vaccines, which comprise a polypeptide as described above in combination with an immunostimulant or adjuvant, are provided. In yet other aspects, the present invention provides pharmaceutical compositions and vaccines comprising a polypeptide encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242 and 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In related aspects, the present invention provides methods for inhibiting the development of breast cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as described above.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

25 BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the differential display PCR products, separated by gel electrophoresis, obtained from cDNA prepared from normal breast tissue (lanes 1 and 2) and from cDNA prepared from breast tumor tissue from the same patient (lanes 3 and 4). The arrow indicates the band corresponding to B18Ag1.

Figure 2 is a northern blot comparing the level of B18Ag1 mRNA in breast tumor tissue (lane 1) with the level in normal breast tissue.

Figure 3 shows the level of B18Ag1 mRNA in breast tumor tissue compared to that in various normal and non-breast tumor tissues as determined by RNase protection assays.

Figure 4 is a genomic clone map showing the location of additional retroviral sequences obtained from ends of XbaI restriction digests (provided in SEQ ID NO:3 - SEQ ID NO:10) relative to B18Ag1.

Figures 5A and 5B show the sequencing strategy, genomic organization and predicted open reading frame for the retroviral element containing B18Ag1.

Figure 6 shows the nucleotide sequence of the representative breast tumor-specific cDNA B18Ag1.

Figure 7 shows the nucleotide sequence of the representative breast tumor-specific cDNA B17Ag1.

Figure 8 shows the nucleotide sequence of the representative breast tumor-specific cDNA B17Ag2.

Figure 9 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag2a.

Figure 10 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag1b.

Figure 11 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag1a.

Figure 12 shows the nucleotide sequence of the representative breast tumor-specific cDNA B11Ag1.

Figure 13 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA3c.

Figure 14 shows the nucleotide sequence of the representative breast tumor-specific cDNA B9CG1.

Figure 15 shows the nucleotide sequence of the representative breast tumor-specific cDNA B9CG3.

Figure 16 shows the nucleotide sequence of the representative breast tumor-specific cDNA B2CA2.

Figure 17 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA1.

5 Figure 18 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA2.

Figure 19 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA3.

10 Figure 20 shows the nucleotide sequence of the representative breast tumor-specific cDNA B4CA1.

Figure 21A depicts RT-PCR analysis of breast tumor genes in breast tumor tissues (lanes 1-8) and normal breast tissues (lanes 9-13) and H₂O (lane 14).

Figure 21B depicts RT-PCR analysis of breast tumor genes in prostate tumors (lane 1, 2), colon tumors (lane 3), lung tumor (lane 4), normal prostate (lane 5),
15 normal colon (lane 6), normal kidney (lane 7), normal liver (lane 8), normal lung (lane 9), normal ovary (lanes 10, 18), normal pancreases (lanes 11, 12), normal skeletal muscle (lane 13), normal skin (lane 14), normal stomach (lane 15), normal testes (lane 16), normal small intestine (lane 17), HBL-100 (lane 19), MCF-12A (lane 20), breast tumors (lanes 21-23), H₂O (lane 24), and colon tumor (lane 25).

20 Figure 22 shows the recognition of a B11Ag1 peptide (referred to as B11-8) by an anti-B11-8 CTL line.

Figure 23 shows the recognition of a cell line transduced with the antigen B11Ag1 by the B11-8 specific clone A1.

25 Figure 24 shows recognition of a lung adenocarcinoma line (LT-140-22) and a breast adenocarcinoma line (CAMA-1) by the B11-8 specific clone A1.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the diagnosis, monitoring and therapy of breast cancer. The compositions described herein include polypeptides, polynucleotides and antibodies.

Polypeptides of the present invention generally comprise at least a portion of a protein that is expressed at a greater level in human breast tumor tissue than in normal breast tissue (i.e., the level of RNA encoding the polypeptide is at least 2-fold higher in tumor tissue). Such polypeptides are referred to herein as breast tumor-specific polypeptides, and cDNA molecules encoding such polypeptides are referred to as breast tumor-specific cDNAs. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of a polypeptide as described above, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or fragments thereof, that are capable of binding to a portion of a polypeptide as described above. Antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies.

Polypeptides within the scope of this invention include, but are not limited to, polypeptides (and epitopes thereof) encoded by a human endogenous retroviral sequence, such as the sequence designated B18Ag1 (Figure 5 and SEQ ID NO:1). Also within the scope of the present invention are polypeptides encoded by other sequences within the retroviral genome containing B18Ag1 (SEQ ID NO: 141). Such sequences include, but are not limited to, the sequences recited in SEQ ID NO:3 - SEQ ID NO:10. B18Ag1 has homology to the *gag* p30 gene of the endogenous human retroviral element S71, as described in Werner et al., *Virology* 174:225-238 (1990) and also shows homology to about thirty other retroviral *gag* genes. As discussed in more detail below, the present invention also includes a number of additional breast tumor-specific polypeptides, such as those encoded by the nucleotide sequences recited in SEQ ID NO: 11-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins containing the sequences recited herein. A

polypeptide comprising an epitope of a protein containing a sequence as described herein may consist entirely of the epitope, or may contain additional sequences. The additional sequences may be derived from the native protein or may be heterologous, and such sequences may (but need not) possess immunogenic or antigenic properties.

5 An "epitope," as used herein is a portion of a polypeptide that is recognized (i.e., specifically bound) by a B-cell and/or T-cell surface antigen receptor. Epitopes may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides derived
10 from the native polypeptide for the ability to react with antigen-specific antisera and/or T-cell lines or clones. An epitope of a polypeptide is a portion that reacts with such antisera and/or T-cells at a level that is similar to the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such screens may generally be performed using methods well known to those of ordinary skill in the art,
15 such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. B-cell and T-cell epitopes may also be predicted via computer analysis. Polypeptides comprising an epitope of a polypeptide that is preferentially expressed in a tumor tissue (with or without additional amino acid sequence) are within the scope of the present invention.

20 The term "polynucleotide(s)," as used herein, means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and corresponding RNA molecules, including HnRNA and mRNA molecules, both sense and anti-sense strands, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. An HnRNA molecule contains
25 introns and corresponds to a DNA molecule in a generally one-to-one manner. An mRNA molecule corresponds to an HnRNA and DNA molecule from which the introns have been excised. A polynucleotide may consist of an entire gene, or any portion thereof. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes
30 all such operable anti-sense fragments.

The compositions and methods of the present invention also encompass variants of the above polypeptides and polynucleotides.

A polypeptide "variant," as used herein, is a polypeptide that differs from the recited polypeptide only in conservative substitutions and/or modifications, such that the antigenic properties of the polypeptide are retained. In a preferred embodiment, variant polypeptides differ from an identified sequence by substitution, deletion or addition of five amino acids or fewer. Such variants may generally be identified by modifying one of the above polypeptide sequences, and evaluating the antigenic properties of the modified polypeptide using, for example, the representative procedures described herein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described below) to the identified polypeptides.

As used herein, a "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. In general, the following groups of amino acids represent conservative changes: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his.

Variants may also, or alternatively, contain other modifications, including the deletion or addition of amino acids that have minimal influence on the antigenic properties, secondary structure and hydrophobic nature of the polypeptide. For example, a polypeptide may be conjugated to a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

A nucleotide "variant" is a sequence that differs from the recited nucleotide sequence in having one or more nucleotide deletions, substitutions or

additions. Such modifications may be readily introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis as taught, for example, by Adelman et al. (*DNA*, 2:183, 1983). Nucleotide variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant nucleotide sequences preferably exhibit at least about 70%, more preferably at least about 80% and most preferably at least about 90% identity (determined as described below) to the recited sequence.

The breast tumor antigens provided by the present invention include variants that are encoded by DNA sequences which are substantially homologous to one or more of the DNA sequences specifically recited herein. "Substantial homology," as used herein, refers to DNA sequences that are capable of hybridizing under moderately stringent conditions. Suitable moderately stringent conditions include prewashing in a solution of 5X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5X SSC, overnight or, in the event of cross-species homology, at 45°C with 0.5X SSC; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. Such hybridizing DNA sequences are also within the scope of this invention, as are nucleotide sequences that, due to code degeneracy, encode an immunogenic polypeptide that is encoded by a hybridizing DNA sequence.

Two nucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acid residues in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment

schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins - Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) Fast and sensitive multiple sequence alignments on a microcomputer *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) Optimal alignments in linear space *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) The neighbor joining method. A new method for reconstructing phylogenetic trees *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy - the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Rapid similarity searches of nucleic acid and protein data banks *Proc. Natl. Acad. Sci. USA* 80:726-730.

15 Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity. In general, polynucleotides encoding all or a portion of the polypeptides described herein may be prepared using any of several techniques. For example, cDNA molecules encoding such polypeptides may be cloned on the basis of the breast tumor-specific expression of the corresponding mRNAs, using differential display PCR. This technique compares the amplified products from RNA template prepared from normal and breast tumor tissue. cDNA may

be prepared by reverse transcription of RNA using a (dT)₁₂AG primer. Following amplification of the cDNA using a random primer, a band corresponding to an amplified product specific to the tumor RNA may be cut out from a silver stained gel and subcloned into a suitable vector (e.g., the T-vector, Novagen, Madison, WI).

5 Polynucleotides encoding all or a portion of the breast tumor-specific polypeptides disclosed herein may be amplified from cDNA prepared as described above using the random primers shown in SEQ ID NO.:87-125.

Alternatively, a polynucleotide encoding a polypeptide as described herein (or a portion thereof) may be amplified from human genomic DNA, or from breast

10 tumor cDNA, via polymerase chain reaction. For this approach, B18Ag1 sequence-specific primers may be designed based on the sequence provided in SEQ ID NO:1, and may be purchased or synthesized. One suitable primer pair for amplification from breast tumor cDNA is (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO:126) and (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127). An amplified portion of

15 B18Ag1 may then be used to isolate the full length gene from a human genomic DNA library or from a breast tumor cDNA library, using well known techniques, such as those described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY (1989). Other sequences within the retroviral genome of which B18Ag1 is a part may be similarly prepared by screening

20 human genomic libraries using B18Ag1-specific sequences as probes. Nucleotides translated into protein from the retroviral genome shown in SEQ ID NO: 141 may then be determined by cloning the corresponding cDNAs, predicting the open reading frames and cloning the appropriate cDNAs into a vector containing a viral promoter, such as T7. The resulting constructs can be employed in a translation reaction, using techniques

25 known to those of skill in the art, to identify nucleotide sequences which result in expressed protein. Similarly, primers specific for the remaining breast tumor-specific polypeptides described herein may be designed based on the nucleotide sequences provided in SEQ ID NO:11-86, 142-298, 301-303, 307, 313, 314, 316 and 317.

Recombinant polypeptides encoded by the DNA sequences described

30 above may be readily prepared from the DNA sequences. For example, supernatants

from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps
5 can be employed to further purify a recombinant polypeptide.

In general, any of a variety of expression vectors known to those of ordinary skill in the art may be employed to express recombinant polypeptides of this invention. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a polynucleotide that
10 encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO.

Such techniques may also be used to prepare polypeptides comprising epitopes or variants of the native polypeptides. For example, variants of a native
15 polypeptide may generally be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis, and sections of the DNA sequence may be removed to permit preparation of truncated polypeptides. Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to
20 those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146 (1963). Equipment for automated synthesis of polypeptides is commercially available from suppliers such as
25 Perkin Elmer/Applied BioSystems Division, Foster City, CA, and may be operated according to the manufacturer's instructions.

In specific embodiments, polypeptides of the present invention encompass amino acid sequences encoded by a polynucleotide having a sequence recited in any one
30 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255,

257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317, and variants of such polypeptides. Polypeptides within the scope of the present invention also include polypeptides (and epitopes thereof) encoded by DNA sequences that hybridize to a sequence recited in any one of SEQ ID NO:1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under stringent conditions, wherein the DNA sequences are at least 80% identical in overall sequence to a recited sequence and wherein RNA corresponding to the nucleotide sequence is expressed at a greater level in human breast tumor tissue than in normal breast tissue. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65°C and two washes of 30 minutes each in 0.2 X SSC, 0.1% SDS at 65°C. Polynucleotides according to the present invention include molecules that encode any of the above polypeptides.

In another aspect of the present invention, antibodies are provided. Such antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one such technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for the antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519 (1976), and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Antibodies may be used, for example, in methods for detecting breast cancer in a patient. Such methods involve using an antibody to detect the presence or absence of a breast tumor-specific polypeptide as described herein in a suitable biological sample. As used herein, suitable biological samples include tumor or normal tissue biopsy, mastectomy, blood, lymph node, serum or urine samples, or other tissue, homogenate, or extract thereof obtained from a patient.

There are a variety of assay formats known to those of ordinary skill in the art for using an antibody to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, the assay may be performed in a Western blot format, wherein a protein preparation from the biological sample is submitted to gel electrophoresis, transferred to a suitable membrane and allowed to react with the antibody. The presence of the antibody on the membrane may then be detected using a suitable detection reagent, as described below.

In another embodiment, the assay involves the use of antibody immobilized on a solid support to bind to the polypeptide and remove it from the remainder of the sample. The bound polypeptide may then be detected using a second antibody or reagent that contains a reporter group. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized antibody after incubation of the antibody with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the antibody is indicative of the reactivity of the sample with the immobilized antibody, and as a result, indicative of the concentration of polypeptide in the sample.

The solid support may be any material known to those of ordinary skill in the art to which the antibody may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose filter or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681.

The antibody may be immobilized on the solid support using a variety of techniques known to those in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the antigen and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a

well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the antibody, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of antibody ranging from about 10 ng to about 1 μ g, and preferably about 100-200 ng, is sufficient to immobilize an adequate amount of polypeptide.

Covalent attachment of antibody to a solid support may also generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the antibody. For example, the antibody may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook (1991) at A12-A13).

In certain embodiments, the assay for detection of polypeptide in a sample is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the biological sample, such that the polypeptide within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a second antibody (containing a reporter group) capable of binding to a different site on the polypeptide is added. The amount of second antibody that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked.

Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.,* incubation

time) is that period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with breast cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include enzymes (such as horseradish peroxidase), substrates, cofactors, inhibitors, dyes, radionuclides, luminescent groups, fluorescent groups and biotin. The conjugation of antibody to reporter group may be achieved using standard methods known to those of ordinary skill in the art.

The second antibody is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound second antibody is then removed and bound second antibody is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of breast cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value established from non-tumor tissue. In one preferred embodiment, the cut-off value is the average mean signal

obtained when the immobilized antibody is incubated with samples from patients without breast cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value may be considered positive for breast cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, p. 106-7 (Little Brown and Co., 1985). Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for breast cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the antibody is immobilized on a membrane, such as nitrocellulose. In the flow-through test, the polypeptide within the sample bind to the immobilized antibody as the sample passes through the membrane. A second, labeled antibody then binds to the antibody-polypeptide complex as a solution containing the second antibody flows through the membrane. The detection of bound second antibody may then be performed as described above. In the strip test format, one end of the membrane to which antibody is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second antibody and to the area of immobilized antibody. Concentration of second antibody at the area of immobilized antibody indicates the presence of breast cancer. Typically, the concentration of second antibody at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of antibody immobilized on the membrane is selected to generate a visually

discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 1 μ g. Such tests can typically be performed with a very small amount of biological sample.

The presence or absence of breast cancer in a patient may also be determined by evaluating the level of mRNA encoding a breast tumor-specific polypeptide as described herein within the biological sample (e.g., a biopsy, mastectomy and/or blood sample from a patient) relative to a predetermined cut-off value. Such an evaluation may be achieved using any of a variety of methods known to those of ordinary skill in the art such as, for example, *in situ* hybridization and amplification by polymerase chain reaction.

For example, polymerase chain reaction may be used to amplify sequences from cDNA prepared from RNA that is isolated from one of the above biological samples. Sequence-specific primers for use in such amplification may be designed based on the sequences provided in any one of SEQ ID NO: 1, 11-86, 142-298 301-303, 307, 313, 314, 316 and 317, and may be purchased or synthesized. In the case of B18Ag1, as noted herein, one suitable primer pair is B18Ag1-2 (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO:126) and B18Ag1-3 (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127). The PCR reaction products may then be separated by gel electrophoresis and visualized according to methods well known to those of ordinary skill in the art. Amplification is typically performed on samples obtained from matched pairs of tissue (tumor and non-tumor tissue from the same individual) or from unmatched pairs of tissue (tumor and non-tumor tissue from different individuals). The amplification reaction is preferably performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the tumor sample as compared to the same dilution of the non-tumor sample is considered positive.

As used herein, the term "primer/probe specific for a polynucleotide" means an oligonucleotide sequence that has at least about 80% identity, preferably at least about 90% and more preferably at least about 95%, identity to the polynucleotide in question, or an oligonucleotide sequence that is anti-sense to a sequence that has at least about 80% identity, preferably at least about 90% and more preferably at least about 95%, identity to the polynucleotide in question. Primers and/or probes which may be usefully employed in the inventive diagnostic methods preferably have at least about 10-40 nucleotides. In a preferred embodiment, the polymerase chain reaction primers comprise at least about 10 contiguous nucleotides of a polynucleotide that encodes one of the polypeptides disclosed herein or that is anti-sense to a sequence that encodes one of the polypeptides disclosed herein. Preferably, oligonucleotide probes for use in the inventive diagnostic methods comprise at least about 15 contiguous oligonucleotides of a polynucleotide that encodes one of the polypeptides disclosed herein or that is anti-sense to a sequence that encodes one of the polypeptides disclosed herein. Techniques for both PCR based assays and *in situ* hybridization assays are well known in the art.

Conventional RT-PCR protocols using agarose and ethidium bromide staining, while important in defining gene specificity, do not lend themselves to diagnostic kit development because of the time and effort required in making them quantitative (i.e., construction of saturation and/or titration curves), and their sample throughput. This problem is overcome by the development of procedures such as real time RT-PCR which allows for assays to be performed in single tubes, and in turn can be modified for use in 96 well plate formats. Instrumentation to perform such methodologies are available from Perkin Elmer/Applied Biosystems Division. Alternatively, other high throughput assays using labeled probes (e.g., digoxigenin) in combination with labeled (e.g., enzyme fluorescent, radioactive) antibodies to such probes can also be used in the development of 96 well plate assays.

In yet another method for determining the presence or absence of breast cancer in a patient, one or more of the breast tumor-specific polypeptides described may be used in a skin test. As used herein, a "skin test" is any assay performed directly on a patient in which a delayed-type hypersensitivity (DTH) reaction (such as swelling,

reddening or dermatitis) is measured following intradermal injection of one or more polypeptides as described above. Such injection may be achieved using any suitable device sufficient to contact the polypeptide or polypeptides with dermal cells of the patient, such as a tuberculin syringe or 1 mL syringe. Preferably, the reaction is measured at least 48 hours after injection, more preferably 48-72 hours.

The DTH reaction is a cell-mediated immune response, which is greater in patients that have been exposed previously to a test antigen (*i.e.*, an immunogenic portion of a polypeptide employed, or a variant thereof). The response may be measured visually, using a ruler. In general, a response that is greater than about 0.5 cm in diameter, preferably greater than about 5.0 cm in diameter, is a positive response, indicative of breast cancer.

The breast tumor-specific polypeptides described herein are preferably formulated, for use in a skin test, as pharmaceutical compositions containing at least one polypeptide and a physiologically acceptable carrier, such as water, saline, alcohol, or a buffer. Such compositions typically contain one or more of the above polypeptides in an amount ranging from about 1 μ g to 100 μ g, preferably from about 10 μ g to 50 μ g in a volume of 0.1 mL. Preferably, the carrier employed in such pharmaceutical compositions is a saline solution with appropriate preservatives, such as phenol and/or Tween 80™.

In other aspects of the present invention, the progression and/or response to treatment of a breast cancer may be monitored by performing any of the above assays over a period of time, and evaluating the change in the level of the response (*i.e.*, the amount of polypeptide or mRNA detected or, in the case of a skin test, the extent of the immune response detected). For example, the assays may be performed every month to every other month for a period of 1 to 2 years. In general, breast cancer is progressing in those patients in whom the level of the response increases over time. In contrast, breast cancer is not progressing when the signal detected either remains constant or decreases with time.

In further aspects of the present invention, the compounds described herein may be used for the immunotherapy of breast cancer. In these aspects, the

compounds (which may be polypeptides, antibodies or polynucleotides) are preferably incorporated into pharmaceutical compositions or vaccines. Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds in combination with an immunostimulant, such as an adjuvant or a liposome (into which the compound is incorporated). An immunostimulant may be any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

Alternatively, a vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. In such vaccines, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749 (1993), and reviewed by

Cohen, *Science* 259:1691-1692 (1993). The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the

induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with a salt. MPL adjuvants are available from Corixa Corporation, Seattle, WA; see patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,091. CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc., Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (e.g., SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immunostimulant and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology (*see, e.g.*, Coombes et al., *Vaccine* 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see, e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA

haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (see Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible

intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcγ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a polypeptide of the present invention (or portion or other variant thereof) such that the polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier

immediately prior to use.

The above pharmaceutical compositions and vaccines may be used, for example, for the therapy of breast cancer in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with breast cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of breast cancer or to treat a patient afflicted with breast cancer. In a preferred embodiment, the compounds are administered either prior to or following surgical removal of primary tumors and/or treatment by administration of radiotherapy and conventional chemotherapeutic drugs. To prevent or slow the development of breast cancer, a pharmaceutical composition or vaccine comprising one or more polypeptides as described herein may be administered to a patient. Alternatively, naked DNA or plasmid or viral vector encoding the polypeptide may be administered. For treating a patient with breast cancer, the pharmaceutical composition or vaccine may comprise one or more polypeptides, antibodies or polynucleotides complementary to DNA encoding a polypeptide as described herein (e.g., antisense RNA or antisense deoxyribonucleotide oligonucleotides).

Routes and frequency of administration, as well as dosage, will vary from individual to individual. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Between 1 and 10 doses may be administered for a 52-week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical

compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 μ g to 5 mg. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

5 Polypeptides disclosed herein may also be employed in adoptive immunotherapy for the treatment of cancer. Adoptive immunotherapy may be broadly classified into either active or passive immunotherapy. In active immunotherapy, treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (for
10 example, tumor vaccines, bacterial adjuvants, and/or cytokines).

In passive immunotherapy, treatment involves the delivery of biologic reagents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T lymphocytes (for
15 example, CD8+ cytotoxic T-lymphocyte, CD4+ T-helper, tumor-infiltrating lymphocytes), killer cells (Natural Killer cells, lymphokine-activated killer cells), B cells, or antigen presenting cells (such as dendritic cells and macrophages) expressing the disclosed antigens. The polypeptides disclosed herein may also be used to generate antibodies or anti-idiotypic antibodies (as in U.S. Patent No. 4,918,164), for passive
20 immunotherapy.

The predominant method of procuring adequate numbers of T-cells for adoptive immunotherapy is to grow immune T-cells *in vitro*. Culture conditions for expanding single antigen-specific T-cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. These *in vitro* culture conditions
25 typically utilize intermittent stimulation with antigen, often in the presence of cytokines, such as IL-2, and non-dividing feeder cells. As noted above, the immunoreactive polypeptides described herein may be used to rapidly expand antigen-specific T cell cultures in order to generate sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage or B-cells, may be pulsed with
30 immunoreactive polypeptides or transfected with a polynucleotide sequence(s), using

standard techniques well known in the art. For cultured T-cells to be effective in therapy, the cultured T-cells must be able to grow and distribute widely and to survive long term *in vivo*. Studies have demonstrated that cultured T-cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al. *Ibid*).

The polypeptides disclosed herein may also be employed to generate and/or isolate tumor-reactive T-cells, which can then be administered to the patient. In one technique, antigen-specific T-cell lines may be generated by *in vivo* immunization with short peptides corresponding to immunogenic portions of the disclosed polypeptides. The resulting antigen specific CD8+ CTL clones may be isolated from the patient, expanded using standard tissue culture techniques, and returned to the patient.

Alternatively, peptides corresponding to immunogenic portions of the polypeptides may be employed to generate tumor reactive T cell subsets by selective *in vitro* stimulation and expansion of autologous T cells to provide antigen-specific T cells which may be subsequently transferred to the patient as described, for example, by Chang et al. (*Crit. Rev. Oncol. Hematol.*, 22(3), 213, 1996).

In another embodiment, syngeneic or autologous dendritic cells may be pulsed with peptides corresponding to at least an immunogenic portion of a polypeptide disclosed herein. The resulting antigen-specific dendritic cells may either be transferred into a patient, or employed to stimulate T cells to provide antigen-specific T cells which may, in turn, be administered to a patient. The use of peptide-pulsed dendritic cells to generate antigen-specific T cells and the subsequent use of such antigen-specific T cells to eradicate tumors in a murine model has been demonstrated by Cheever et al. ("Therapy With Cultured T Cells: Principles Revisited," *Immunological Reviews*, 157:177, 1997).

Additionally vectors expressing the disclosed polynucleotides may be introduced into stem cells taken from the patient and clonally propagated *in vitro* for autologous transplant back into the same patient. In one embodiment, cells of the immune system, such as T cells, may be isolated from the peripheral blood of a patient, using a commercially available cell separation system, such as CellPro Incorporated's (Bothell,

WA) CEPRATE™ system (see U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). The separated cells are stimulated with one or more of the immunoreactive polypeptides contained within a delivery vehicle, such as a microsphere, to provide antigen-specific T cells. The population of tumor antigen-specific T cells is then expanded using standard techniques and the cells are administered back to the patient.

The following Examples are offered by way of illustration and not by way of limitation.

10

EXAMPLES

EXAMPLE 1

PREPARATION OF BREAST TUMOR-SPECIFIC CDNAS USING

15

DIFFERENTIAL DISPLAY RT-PCR

This Example illustrates the preparation of cDNA molecules encoding breast tumor-specific polypeptides using a differential display screen.

A. Preparation of B18Ag1 cDNA and Characterization of mRNA Expression

20

Tissue samples were prepared from breast tumor and normal tissue of a patient with breast cancer that was confirmed by pathology after removal from the patient. Normal RNA and tumor RNA was extracted from the samples and mRNA was isolated and converted into cDNA using a (dT)₁₂AG (SEQ ID NO:130) anchored 3' primer. Differential display PCR was then executed using a randomly chosen primer (CTTCAACCTC) (SEQ ID NO:103). Amplification conditions were standard buffer containing 1.5 mM MgCl₂, 20 pmol of primer, 500 pmol dNTP, and 1 unit of *Taq* DNA polymerase (Perkin-Elmer, Branchburg, NJ). Forty cycles of amplification were performed using 94°C denaturation for 30 seconds, 42°C annealing for 1 minute, and 72°C extension for 30 seconds. An RNA fingerprint containing 76 amplified products was

obtained. Although the RNA fingerprint of breast tumor tissue was over 98% identical to that of the normal breast tissue, a band was repeatedly observed to be specific to the RNA fingerprint pattern of the tumor. This band was cut out of a silver stained gel, subcloned into the T-vector (Novagen, Madison, WI) and sequenced.

5 The sequence of the cDNA, referred to as B18Ag1, is provided in SEQ ID NO:1. A database search of GENBANK and EMBL revealed that the B18Ag1 fragment initially cloned is 77% identical to the endogenous human retroviral element S71, which is a truncated retroviral element homologous to the Simian Sarcoma Virus (SSV). S71 contains an incomplete *gag* gene, a portion of the *pol* gene and an LTR-like structure at 10 the 3' terminus (see Werner et al., *Virology* 174:225-238 (1990)). B18Ag1 is also 64% identical to SSV in the region corresponding to the P30 (*gag*) locus. B18Ag1 contains three separate and incomplete reading frames covering a region which shares considerable homology to a wide variety of *gag* proteins of retroviruses which infect mammals. In addition, the homology to S71 is not just within the *gag* gene, but spans 15 several kb of sequence including an LTR.

B18Ag1-specific PCR primers were synthesized using computer analysis guidelines. RT-PCR amplification (94°C, 30 seconds; 60°C → 42°C, 30 seconds; 72°C, 30 seconds for 40 cycles) confirmed that B18Ag1 represents an actual mRNA sequence present at relatively high levels in the patient's breast tumor tissue. The primers used in 20 amplification were B18Ag1-1 (CTG CCT GAG CCA CAA ATG) (SEQ ID NO:128) and B18Ag1-4 (CCG GAG GAG GAA GCT AGA GGA ATA) (SEQ ID NO:129) at a 3.5 mM magnesium concentration and a pH of 8.5, and B18Ag1-2 (ATG GCT ATT TTC GGG GCC TGA CA) (SEQ ID NO:126) and B18Ag1-3 (CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127) at 2 mM magnesium at pH 9.5. The same experiments 25 showed exceedingly low to nonexistent levels of expression in this patient's normal breast tissue (see Figure 1). RT-PCR experiments were then used to show that B18Ag1 mRNA is present in nine other breast tumor samples (from Brazilian and American patients) but absent in, or at exceedingly low levels in, the normal breast tissue corresponding to each cancer patient. RT-PCR analysis has also shown that the B18Ag1 30 transcript is not present in various normal tissues (including lymph node, myocardium

and liver) and present at relatively low levels in PBMC and lung tissue. The presence of B18Ag1 mRNA in breast tumor samples, and its absence from normal breast tissue, has been confirmed by Northern blot analysis, as shown in Figure 2.

The differential expression of B18Ag1 in breast tumor tissue was also confirmed by RNase protection assays. Figure 3 shows the level of B18Ag1 mRNA in various tissue types as determined in four different RNase protection assays. Lanes 1-12 represent various normal breast tissue samples, lanes 13-25 represent various breast tumor samples; lanes 26-27 represent normal prostate samples; lanes 28-29 represent prostate tumor samples; lanes 30-32 represent colon tumor samples; lane 33 represents normal aorta; lane 34 represents normal small intestine; lane 35 represents normal skin, lane 36 represents normal lymph node; lane 37 represents normal ovary; lane 38 represents normal liver; lane 39 represents normal skeletal muscle; lane 40 represents a first normal stomach sample, lane 41 represents a second normal stomach sample; lane 42 represents a normal lung; lane 43 represents normal kidney; and lane 44 represents normal pancreas. Interexperimental comparison was facilitated by including a positive control RNA of known β -actin message abundance in each assay and normalizing the results of the different assays with respect to this positive control.

RT-PCR and Southern Blot analysis has shown the B18Ag1 locus to be present in human genomic DNA as a single copy endogenous retroviral element. A genomic clone of approximately 12-18 kb was isolated using the initial B18Ag1 sequence as a probe. Four additional subclones were also isolated by XbaI digestion. Additional retroviral sequences obtained from the ends of the XbaI digests of these clones (located as shown in Figure 4) are shown as SEQ ID NO:3 - SEQ ID NO:10, where SEQ ID NO:3 shows the location of the sequence labeled 10 in Figure 4, SEQ ID NO:4 shows the location of the sequence labeled 11-29, SEQ ID NO:5 shows the location of the sequence labeled 3, SEQ ID NO:6 shows the location of the sequence labeled 6, SEQ ID NO:7 shows the location of the sequence labeled 12, SEQ ID NO:8 shows the location of the sequence labeled 13, SEQ ID NO:9 shows the location of the sequence labeled 14 and SEQ ID NO:10 shows the location of the sequence labeled 11-

Subsequent studies demonstrated that the 12-18 kb genomic clone contains a retroviral element of about 7.75 kb, as shown in Figures 5A and 5B. The sequence of this retroviral element is shown in SEQ ID NO: 141. The numbered line at the top of Figure 5A represents the sense strand sequence of the retroviral genomic clone. The box below this line shows the position of selected restriction sites. The arrows depict the different overlapping clones used to sequence the retroviral element. The direction of the arrow shows whether the single-pass subclone sequence corresponded to the sense or anti-sense strand. Figure 5B is a schematic diagram of the retroviral element containing B18Ag1 depicting the organization of viral genes within the element. The open boxes correspond to predicted reading frames, starting with a methionine, found throughout the element. Each of the six likely reading frames is shown, as indicated to the left of the boxes, with frames 1-3 corresponding to those found on the sense strand.

Using the cDNA of SEQ ID NO:1 as a probe, a longer cDNA was obtained (SEQ ID NO:227) which contains minor nucleotide differences (less than 1%) compared to the genomic sequence shown in SEQ ID NO:141.

B. Preparation of cDNA Molecules Encoding Other Breast Tumor-Specific Polypeptides

Normal RNA and tumor RNA was prepared and mRNA was isolated and converted into cDNA using a (dT)₁₂AG anchored 3' primer, as described above. Differential display PCR was then executed using the randomly chosen primers of SEQ ID NO: 87-125. Amplification conditions were as noted above, and bands observed to be specific to the RNA fingerprint pattern of the tumor were cut out of a silver stained gel, subcloned into either the T-vector (Novagen, Madison, WI) or the pCRII vector (Invitrogen, San Diego, CA) and sequenced. The sequences are provided in SEQ ID NO:11 - SEQ ID NO:86. Of the 79 sequences isolated, 67 were found to be novel (SEQ ID NO:11-26 and 28-77) (see also Figures 6-20).

An extended DNA sequence (SEQ ID NO: 290) for the antigen B15Ag1 (originally identified partial sequence provided in SEQ ID NO: 27) was obtained in further studies. Comparison of the sequence of SEQ ID NO: 290 with those in the gene bank as described above, revealed homology to the known human β -A activin gene.

Further studies led to the isolation of the full-length cDNA sequence for the antigen B21GT2 (also referred to as B311D; originally identified partial cDNA sequence provided in SEQ ID NO: 56). The full-length sequence is provided in SEQ ID NO: 307, with the corresponding amino acid sequence being provided in SEQ ID NO: 308.

5 Further studies led to the isolation of a splice variant of B311D. The B311D clone of SEQ ID NO: 316 was sequenced and a XhoI/NotI fragment from this clone was gel purified and 32P-cDTP labeled by random priming for use as a probe for further screening to obtain additional B311D gene sequence. Two fractions of a human breast tumor cDNA bacterial library were screened using standard techniques. One of the
10 clones isolated in this manner yielded additional sequence which includes a poly A+ tail. The determined cDNA sequence of this clone (referred to as B311D_BT1_1A) is provided in SEQ ID NO: 317. The sequences of SEQ ID NO: 316 and 317 were found to share identity over a 464 bp region, with the sequences diverging near the poly A+ sequence of SEQ ID NO: 317.

15 Subsequent studies identified an additional 146 sequences (SEQ ID NOS:142-289), of which 115 appeared to be novel (SEQ ID NOS:142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288 and 291). To the best of the inventors' knowledge none of the previously
20 identified sequences have heretofore been shown to be expressed at a greater level in human breast tumor tissue than in normal breast tissue.

In further studies, several different splice forms of the antigen B11Ag1 (also referred to as B305D) were isolated, with each of the various splice forms containing slightly different versions of the B11Ag1 coding frame. Splice junction
25 sequences define individual exons which, in various patterns and arrangements, make up the various splice forms. Primers were designed to examine the expression pattern of each of the exons using RT-PCR as described below. Each exon was found to show the same expression pattern as the original B11Ag1 clone, with expression being breast tumor-, normal prostate- and normal testis-specific. The determined cDNA sequences
30 for the isolated protein coding exons are provided in SEQ ID NO: 292-298, respectively.

The predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292 and 298 are provided in SEQ ID NO: 299 and 300. Additional studies using rapid amplification of cDNA ends (RACE), a 5' specific primer to one of the splice forms of B11Ag1 provided above and a breast adenocarcinoma, led to the isolation of three additional, related, splice forms referred to as isoforms B11C-15, B11C-8 and B11C-9,16. The determined cDNA sequences for these isoforms are provided in SEQ ID NO: 301-303, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 304-306.

In subsequent studies on B305D isoform A (cDNA sequence provided in SEQ ID NO: 292), the cDNA sequence (provided in SEQ ID NO: 313) was found to contain an additional guanine residue at position 884, leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in SEQ ID NO: 314. This frameshift generates a protein sequence (provided in SEQ ID NO: 315) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

EXAMPLE 2

PREPARATION OF B18AG1 DNA FROM HUMAN GENOMIC DNA

This Example illustrates the preparation of B18Ag1 DNA by amplification from human genomic DNA.

B18Ag1 DNA may be prepared from 250 ng human genomic DNA using 20 pmol of B18Ag1 specific primers, 500 pmol dNTPS and 1 unit of *Taq* DNA polymerase (Perkin Elmer, Branchburg, NJ) using the following amplification parameters: 94°C for 30 seconds denaturing, 30 seconds 60°C to 42°C touchdown annealing in 2°C increments every two cycles and 72°C extension for 30 seconds. The last increment (a 42°C annealing temperature) should cycle 25 times. Primers were selected using computer analysis. Primers synthesized were B18Ag1-1, B18Ag1-2, B18Ag1-3, and B18Ag1-4. Primer pairs that may be used are 1+3, 1+4, 2+3, and 2+4.

Following gel electrophoresis, the band corresponding to B18Ag1 DNA may be excised and cloned into a suitable vector.

EXAMPLE 3

5 PREPARATION OF B18Ag1 DNA FROM BREAST TUMOR CDNA

This Example illustrates the preparation of B18Ag1 DNA by amplification from human breast tumor cDNA.

First strand cDNA is synthesized from RNA prepared from human breast
10 tumor tissue in a reaction mixture containing 500 ng poly A+ RNA, 200 pmol of the primer (T)₁₂AG (i.e., TTT TTT TTT TTT AG) (SEQ ID NO: 130), 1X first strand reverse transcriptase buffer, 6.7 mM DTT, 500 mmol dNTPs, and 1 unit AMV or MMLV reverse transcriptase (from any supplier, such as Gibco-BRL (Grand Island, NY)) in a final volume of 30 µl. After first strand synthesis, the cDNA is diluted approximately 25
15 fold and 1 µl is used for amplification as described in Example 2. While some primer pairs can result in a heterogeneous population of transcripts, the primers B18Ag1-2 (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO: 126) and B18Ag1-3 (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO: 127) yield a single 151 bp amplification product.

20

EXAMPLE 4

IDENTIFICATION OF B-CELL AND T-CELL EPITOPES OF B18Ag1

This Example illustrates the identification of B18Ag1 epitopes.

25

The B18Ag1 sequence can be screened using a variety of computer algorithms. To determine B-cell epitopes, the sequence can be screened for hydrophobicity and hydrophilicity values using the method of Hopp, *Prog. Clin. Biol. Res.* 172B:367-77 (1985) or, alternatively, Cease et al., *J. Exp. Med.* 164:1779-84 (1986) or Spouge et al., *J. Immunol.* 138:204-12 (1987). Additional Class II MHC (antibody or
30 B-cell) epitopes can be predicted using programs such as AMPHI (e.g., Margalit et al., J.

Immunol. 138:2213 (1987)) or the methods of Rothbard and Taylor (*e.g.*, *EMBO J.* 7:93 (1988)).

Once peptides (15-20 amino acids long) are identified using these techniques, individual peptides can be synthesized using automated peptide synthesis equipment (available from manufacturers such as Perkin Elmer/Applied Biosystems Division, Foster City, CA) and techniques such as Merrifield synthesis. Following synthesis, the peptides can be used to screen sera harvested from either normal or breast cancer patients to determine whether patients with breast cancer possess antibodies reactive with the peptides. Presence of such antibodies in breast cancer patient would confirm the immunogenicity of the specific B-cell epitope in question. The peptides can also be tested for their ability to generate a serologic or humoral immune response in animals (mice, rats, rabbits, chimps etc.) following immunization *in vivo*. Generation of a peptide-specific antiserum following such immunization further confirms the immunogenicity of the specific B-cell epitope in question.

To identify T-cell epitopes, the B18Ag1 sequence can be screened using different computer algorithms which are useful in identifying 8-10 amino acid motifs within the B18Ag1 sequence which are capable of binding to HLA Class I MHC molecules. (*see, e.g.*, Rammensee et al., *Immunogenetics* 41:178-228 (1995)). Following synthesis such peptides can be tested for their ability to bind to class I MHC using standard binding assays (*e.g.*, Sette et al., *J. Immunol.* 153:5586-92 (1994)) and more importantly can be tested for their ability to generate antigen reactive cytotoxic T-cells following *in vitro* stimulation of patient or normal peripheral mononuclear cells using, for example, the methods of Bakker et al., *Cancer Res.* 55:5330-34 (1995); Visseren et al., *J. Immunol.* 154:3991-98 (1995); Kawakami et al., *J. Immunol.* 154:3961-68 (1995); and Kast et al., *J. Immunol.* 152:3904-12 (1994). Successful *in vitro* generation of T-cells capable of killing autologous (bearing the same Class I MHC molecules) tumor cells following *in vitro* peptide stimulation further confirms the immunogenicity of the B18Ag1 antigen. Furthermore, such peptides may be used to generate murine peptide and B18Ag1 reactive cytotoxic T-cells following *in vivo* immunization in mice rendered

specifically lyse target cells in a standard 51-Cr release assay. As shown in Fig. 22, the bulk culture line demonstrated strong recognition of the B11-8 peptide with weaker recognition of the peptide B11-1.

A clone from this CTL line was isolated following rapid expansion using the monoclonal antibody OKT3 and human IL-2. As shown in Fig. 23, this clone (referred to as A1), in addition to being able to recognize specific peptide, recognized JY LCL transduced with the B11Ag1 gene. This data demonstrates that B11-8 is a naturally processed epitope of the B11Ag1 gene. In addition these T cells were further found to recognize and lyse, in an HLA-A2 restricted manner, an established tumor cell line naturally expressing B11Ag1 (Fig. 24). The T cells strongly recognize a lung adenocarcinoma (LT-140-22) naturally expressing B11Ag1 transduced with HLA-A2, as well as an A2+ breast carcinoma (CAMA-1) transduced with B11Ag1, but not untransduced lines or another negative tumor line (SW620).

These data clearly demonstrate that these human T cells recognize not only B11-specific peptides but also transduced cells, as well as naturally expressing tumor lines.

CTL lines raised against the antigens B11-5 and B11-12, using the procedures described above, were found to recognize corresponding peptide-coated targets.

Example 6

CHARACTERIZATION OF BREAST TUMOR GENES DISCOVERED BY
DIFFERENTIAL DISPLAY PCR

5 The specificity and sensitivity of the breast tumor genes discovered by differential display PCR were determined using RT-PCR. This procedure enabled the rapid evaluation of breast tumor gene mRNA expression semiquantitatively without using large amounts of RNA. Using gene specific primers, mRNA expression levels in a variety of tissues were examined, including 8 breast tumors, 5 normal breasts, 2 prostate
10 tumors, 2 colon tumors, 1 lung tumor, and 14 other normal adult human tissues, including normal prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach and testes.

To ensure the semiquantitative nature of the RT-PCR, β -actin was used as internal control for each of the tissues examined. Serial dilutions of the first strand
15 cDNAs were prepared and RT-PCR assays performed using β -actin specific primers. A dilution was then selected that enabled the linear range amplification of β -actin template, and which was sensitive enough to reflect the difference in the initial copy number. Using this condition, the β -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and
20 by assuring a negative result when using first strand cDNA that was prepared without adding reverse transcriptase.

Using gene specific primers, the mRNA expression levels were determined in a variety of tissues. To date, 38 genes have been successfully examined by RT-PCR, five of which exhibit good specificity and sensitivity for breast tumors
25 (B15AG-1, B31GA1b, B38GA2a, B11A1a and B18AG1a). Figures 21A and 21B depict the results for three of these genes: B15AG-1 (SEQ ID NO:27), B31GA1b (SEQ ID NO:148) and B38GA2a (SEQ ID NO. 157). Table I summarizes the expression level of all the genes tested in normal breast tissue and breast tumors, and also in other tissues.

TABLE I

Percentage of Breast Cancer Antigens that are Expressed in Various Tissues

5	Over-expressed in Breast Tumors	84%
	Breast Tissues	
	Equally Expressed in Normals and Tumor	16%
10	Over-expressed in Breast Tumors but not in any Normal Tissues	9%
	Other Tissues	
	Over-expressed in Breast Tumors but Expressed in Some Normal Tissues	30%
15	Over-expressed in Breast Tumors but Equally Expressed in All Other Tissues	61%

20 From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purpose of illustration, various modifications may be made without deviating from the spirit and scope of the invention.

CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(c) complements of sequences of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NOs: 299, 300, 304-306, 308 and 315.

4. An isolated polynucleotide encoding at least 15 amino acid

residues of a protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing sequences.

10

5. An isolated polynucleotide encoding a protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing sequences.

15

6. An isolated polynucleotide, comprising a sequence recited in any

20 one of SEQ ID Nos: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

25

7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions.

30

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.
9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.
10. A host cell transformed or transfected with an expression vector according to claim 9.
11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences.
12. A fusion protein, comprising at least one polypeptide according to claim 1.
13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
14. A fusion protein according to claim 12, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

17. A pharmaceutical composition, comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to

claim 18.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii);
in combination with an immunostimulant.

26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient,

comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (a) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

10 (c) complements of sequences encoded by a polynucleotide recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

and thereby inhibiting the development of a cancer in the patient.

15 30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is breast cancer.

20 (c)

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

25 (i) polynucleotides recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

30

33. A method according to claim 32, wherein the biological sample is

blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

35. A method for stimulating and/or expanding T cells specific for a protein, comprising contacting T cells with at least one component selected from the group consisting of:

10 (a) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

15 (ii) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

20 (c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

30

38. A method for inhibiting the development of a cancer in a patient,

comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that expresses a polypeptide of (i);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(2) sequences that hybridize to a sequence recited in

any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

- (3) complements of sequences of (1) or (2);
- (ii) polynucleotides encoding a polypeptide of (i); and
- 5 (iii) antigen presenting cells that express a polypeptide of (i);

such that T cells proliferate;

- (b) cloning at least one proliferated cell to provide cloned T cells;
- and

- 10 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 15 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;
- 20 (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

25 41. A method according to claim 40, wherein the binding agent is an antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

30

43. A method according to claim 40, wherein the cancer is breast

cancer.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- 5 (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the
15 amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

20 46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

47. A method according to claim 44, wherein the cancer is a breast
25 cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 30 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence

recited in any one of SEQ ID NO: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

5 (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value; and therefrom determining the presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of
10 polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

50. A method according to claim 48, wherein the amount of
15 polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an
20 oligonucleotide that hybridizes to a polynucleotide that encodes a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that
25 hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer
30 in the patient.

52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

- 10 (a) one or more antibodies according to claim 11; and
(b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

15

56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

57. A kit according to claim 54, wherein the reporter group is
20 selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

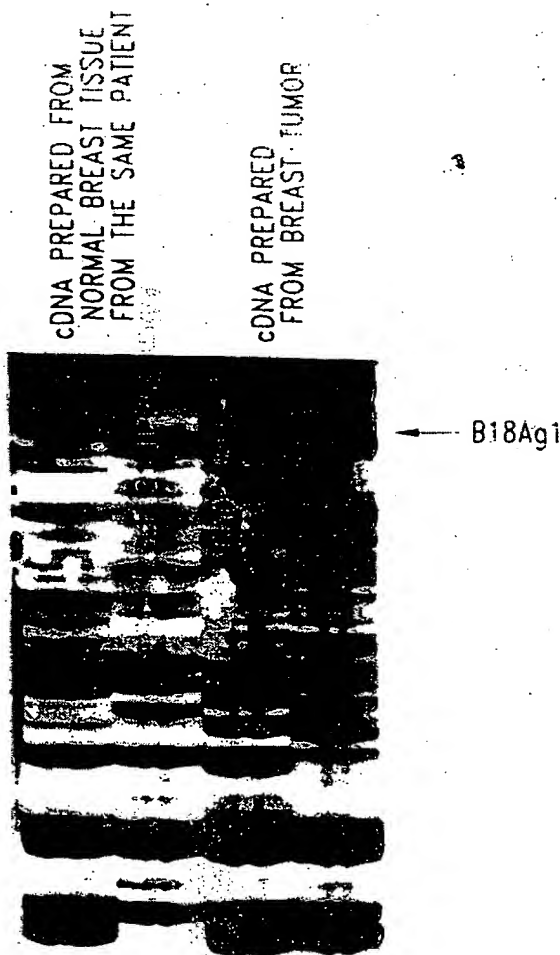
58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a
25 protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a
30 complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID Nos: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

60. A diagnostic kit, comprising:

- (a) an oligonucleotide according to claim 59; and
10 (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

1/25



2/25

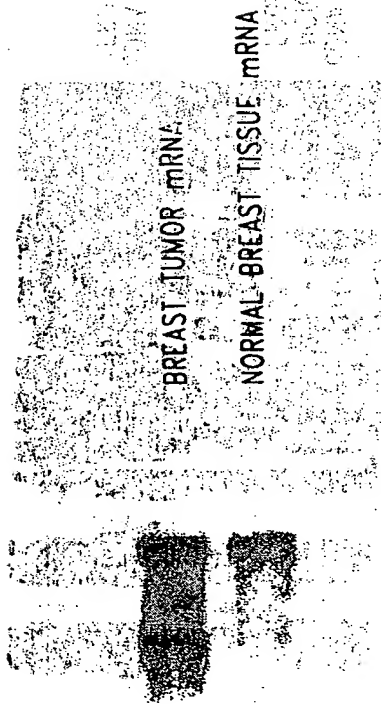


Fig. 2

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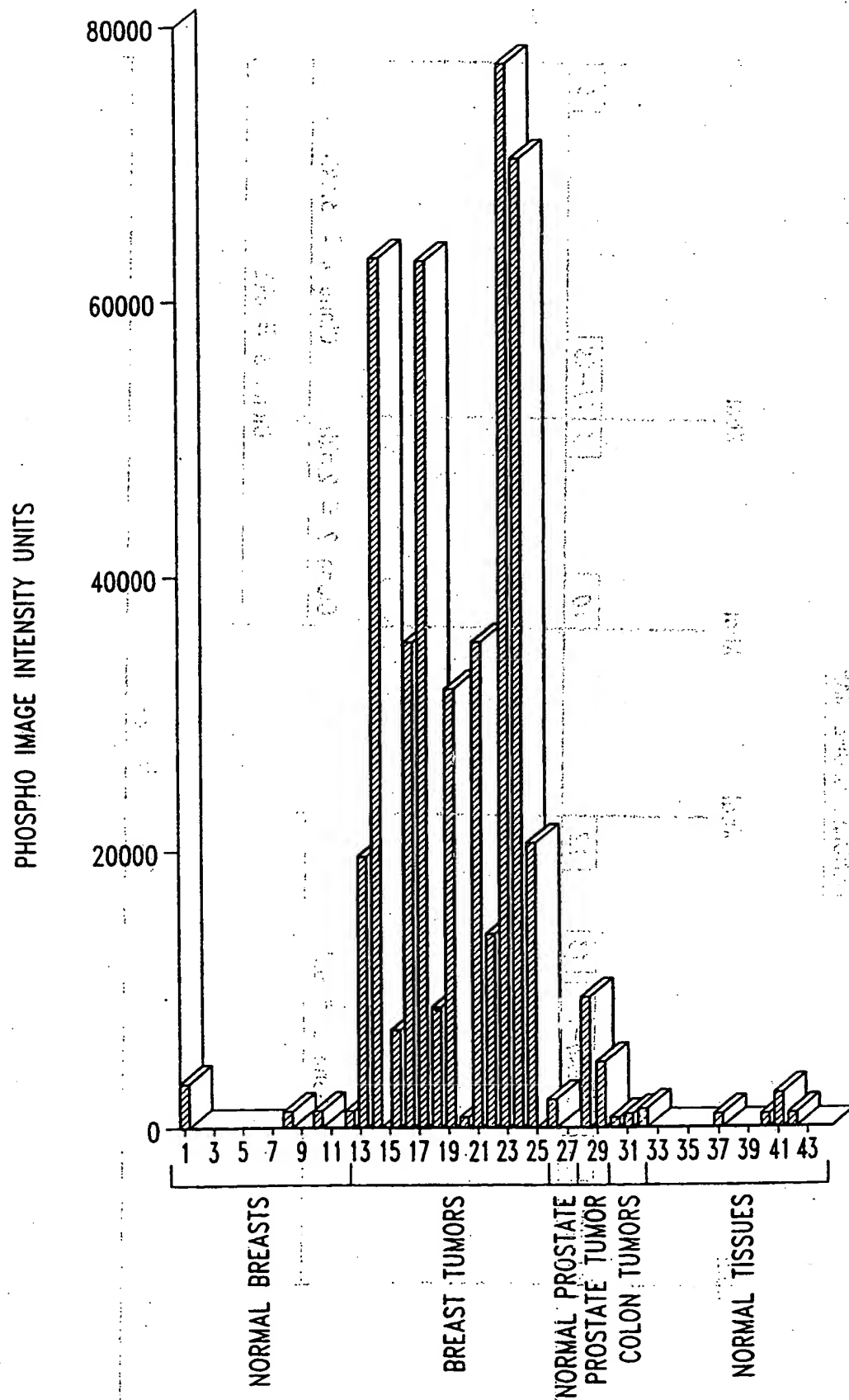


Fig. 3

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GENOMIC CLONE MAP

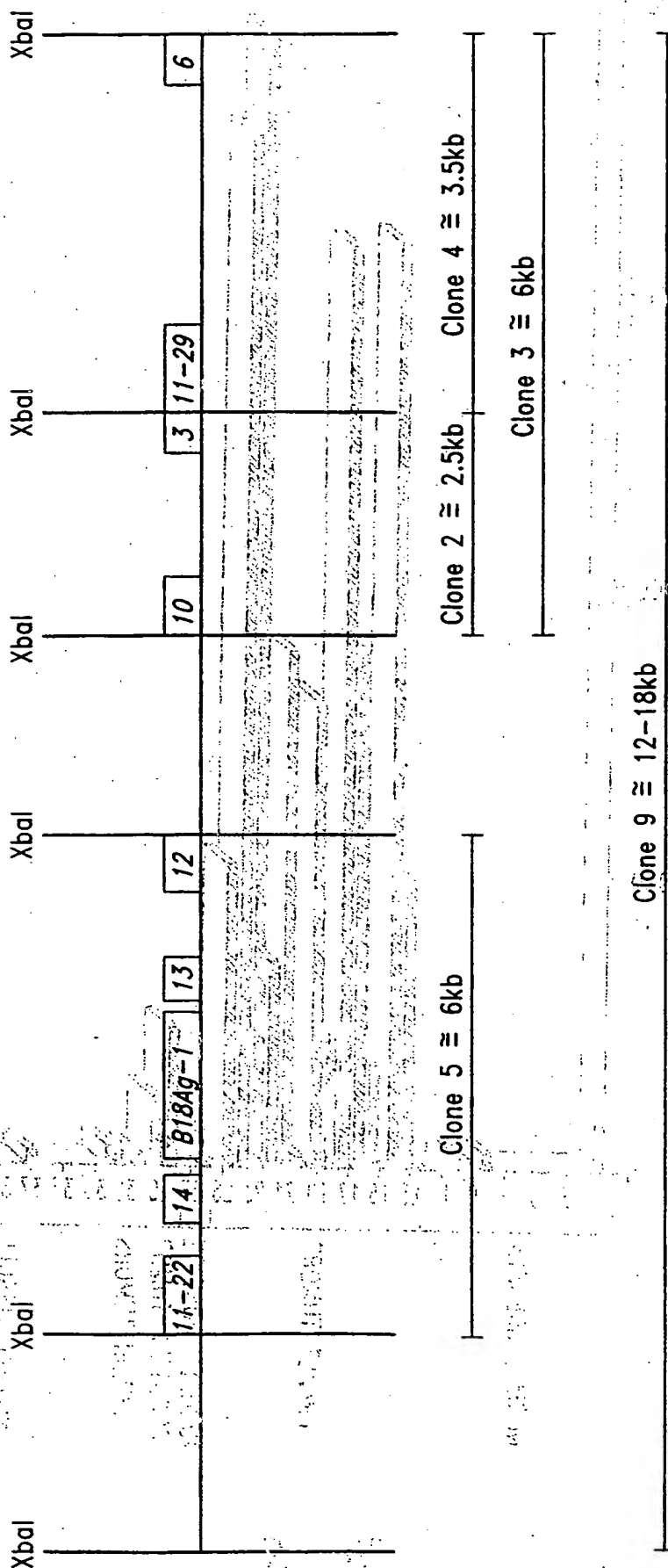
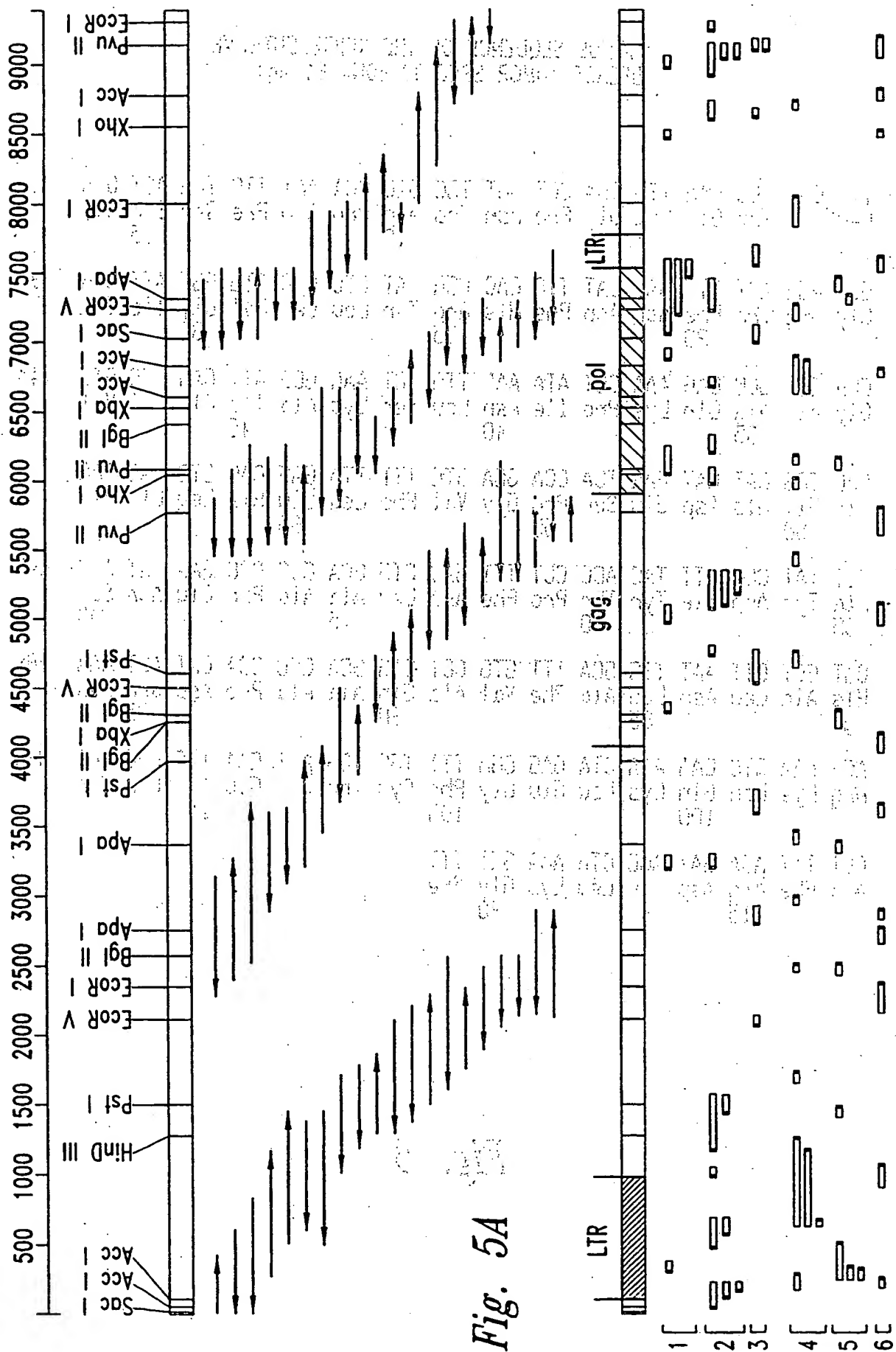


Fig. 4

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B18Ag1

TTA	GAG	ACC	CAA	TTG	GGA	CCT	AAT	TGG	GAC	CCA	AAT	TTC	TCA	AGT	GGA	48
Leu	Glu	Thr	Gln	Leu	Gly	Pro	Asn	Trp	Asp	Pro	Asn	Phe	Ser	Ser	Gly	
1				5				10						15		
GGG	AGA	ACT	TTT	GAC	GAT	TTC	CAC	CGG	TAT	CTC	CTC	GTG	GGT	ATT	CAG	96
Gly	Arg	Thr	Phe	Asp	Asp	Phe	His	Arg	Tyr	Leu	Leu	Val	Gly	Ile	Gln	
			20					25					30			
GGA	GCT	GCC	CAG	AAA	CCT	ATA	AAC	TTG	TCT	AAG	GCG	ATT	GAA	GTC	GTC	144
Gly	Ala	Ala	Gln	Lys	Pro	Ile	Asn	Leu	Ser	Lys	Ala	Ile	Glu	Val	Val	
			35				40					45				
CAG	GGG	CAT	GAT	GAG	TCA	CCA	GGA	GTG	TTT	TTA	GAG	CAC	CTC	CAG	GAG	192
Gln	Gly	His	Asp	Glu	Ser	Pro	Gly	Val	Phe	Leu	Glu	His	Leu	Gln	Glu	
	50					55					60					
GCT	TAT	CGG	ATT	TAC	ACC	CCT	TTT	GAC	CTG	GCA	GCC	CCC	GAA	AAT	AGC	240
Ala	Tyr	Arg	Ile	Tyr	Thr	Pro	Phe	Asp	Leu	Ala	Ala	Pro	Glu	Asn	Ser	
65					70				75					80		
CAT	GCT	GTT	AAT	TTG	GCA	TTT	GTG	GCT	CAG	GCA	GCC	CCA	GAT	AGT	AAA	288
His	Ala	Leu	Asn	Leu	Ala	Phe	Val	Ala	Gln	Ala	Ala	Pro	Asp	Ser	Lys	
			85					90						95		
AGG	AAA	CTC	CAA	AAA	CTA	GAG	GGA	TTT	TGC	TGG	AAT	GAA	TAC	CAG	TCA	336
Arg	Lys	Leu	Gln	Lys	Leu	Glu	Gly	Phe	Cys	Trp	Asn	Glu	Tyr	Gln	Ser	
			100					105					110			
GCT	TTT	AGA	GAT	AGC	CTA	AAA	GGT	TTT								363
Ala	Phe	Arg	Asp	Ser	Leu	Lys	Gly	Phe								
		115					120									

Fig. 6

7/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B17Ag1

GC TGGGCACAGT GGCTCATACC TGTATCCTG ACCGTTTCAG AGGCTCAGGT 60
CG CTGAGCCCA AGATTTCAG ACTAGTCTGG GTAACATAGT GAGACCCTAT 120
AA AAATAAAAAA ATGAGCCTGG TGTAGTGGCA CACACCAGCT GAGGAGGGAG 180
CT AGGAGA 196

Fig. 7

8/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B17Ag2

GC TTGGGGGCTC TGACTAGAAA TTCAAGGAAC CTGGGATTCA AGTCCAAGTG 60
AC TTACACTGTG GNCTCCAATA AACTGCTTCT TTCCTATTCC CTCTCTATTA 120
AA GGAAAACGAT GTCTGTGTAT AGCCAAGTCA GNTATCCTAA AAGGAGATAC 180
AT TAAATATCAG AATGTAAAAC CTGGGAACCA GGTTCACAGC CTGGGATTAA 240
CA AGAAGACTGA ACAGTACTAC TGTGAAAAGC CCGAAGNGGC AATATGTTCA 300
TT GAAGGATGGC TGGGAGAATG AATGCTCTGT CCCCAGTCC CAAGCTCACT 360
CT CCTTTATAGC CTAGGAGA 388

Fig. 8

9/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag2a

GC CTATAATCAT GTTTCTCATT ATTTTCACAT TTTATTAACC AATTTCTGTT 60
AA AATATGAGGG AAATATATGA AACAGGGAGG CAATGTTTCA ATAATTGATC 120
TG ATTTCTACAT CAGATGCTCT TTCCTTTCCT GTTTATTTC TTTTATTTC 180
GG TCGAATGTAA TAGCTTTGTT TCAAGAGAGA GTTTTGGCAG TTTCTGTAGC 240
CT GCTCATGTCT CCAGGCATCT ATTTGCACTT TAGGAGGTGT CGTGGGAGAC 300
CT ATTTTTTCCA TATTGGGCA ACTACTA 337

Fig. 9

10/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag1b

GC CATACAGTGC CTTTCCATTT ATTAAACCCC CACCTGAACG GCATAAACTG 60
GC TGGTGTTTTT TACTGTAAAC AATAAGGAGA CTTTGCTCTT CATTAAACC 120
AT TTCATATTTT ACGCTCGAGG GTTTTTACCG GTTCCTTTTT AACTCCTTA 180
TT TAAGTCGTTT GGAACAAGAT ATTTTTTCTT TCCTGGCAGC TTTAACATT 240
TT TGTGCTGCGG GGAAGTCTGG TCACTGTTTC TCACAGTTGC AAATCAAGGC 300
CC AAGAAAAAAA AATTTTTTTG TTTTATTGTA AACTGGACCG GATAAACGGT 360
CG GCTGCTGTAT ATAGTTTTAA ATGGTTTATT GCACCTCCTT AAGTTGCACT 420
GG GGGGNTTTTG NATAGAAAGT NTTTANTCAC ANAGTCACAG GGACTTTTNT 480
NA CTGAGCTAAA AAGGGCTGNT TTTGGGTTGG GGGCAGATGA AGGCTCACAG 540
TC TCTTAGAGGG GGGAACTNCT A 571

Fig. 10

11/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag1a

TA ATA ACTTAAA TATATTTTGA TCACCCACTG GGGTGATAAG ACAATAGATA 60
TT TCCAAAAGC ATAAACCAA AGTATCATAC CAAACCAAT TCATACTGCT 120
CC GCACTGAAAC TTCACCTTCT AACTGTCTAG CTAACCAAT TCTACCCTTC 180
GG TGGTGCTCA CTACTCTTTT TTTTTTTTTT TTNTTTTGG AGATGGAGTC 240
CA GCCCAGGGGT GGAGTACAAT GGCACAACCT CAGCTCACTG NAACCTCCGC 300
TT CATGAGATTC TCCTGNTTCA GCCITCCCAG TAGCTGGGAC TACAGGTGTG 360
TG CCTGGNTAAT CTTTTTNGT TTTNGGGTAG AGATGGGGGT TTTACATGTT 420
TG GTNTCGAACT CCTGACCTCA AGTGATCCAC GCACCTCAGG CTCCCAAAGT 480
TA CAGACATGAG CCACTGNGCC CAGNCCTGGT GCATGCTCAC TTCTCTAGGC 540
548

Fig. 11

12/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B11Ag1

TG CACATGCAGA ATATTCTATC GGTACTTCAG CTATTACTCA TTTTGATGGC 60
AG CCTATCCTCA AGATGAGTAT TTAGAAAGAA TTGATTTAGC GATAGACCAA 120
GC ACTCTGACTA CACGAAATTG TTCAGATGTG ATGGATTTAT GACAGTTGAT 180
GA GATTATTAAG TGATTATTTT AAAGGGAATC CATTAAATCC AGAATATCTT 240
TC AAGATGATAT AGAAATAGAA CAGAAAGAGA CTACAAATGA AGATGTATCA 300
TA TTGAAGAGCC TATAGTAGAA AATGAATTAG CTGCATTTAT TAGCCTTACA 360
TT TTCCTGATGA ATCTTATATT CAGCCATCSA CATAGCATTG CCTGATGGGC 420
GA ATAATAGAAA CTGGGTGCGG GGCTATTGAT GAATTCATCC NCAGTAAATT 480
AC AAAATATAAC TCGATTGCAT TTGGATGATG GAATACTAAA TCTGGCAAAA 540
GG AGCTACTAGT AACCTCTCTT TTTGAGATGC AAAATTTTCT TTTAGGGTTT 600
CT ACTTTACGGA TATTGGAGCA TAACGGGA 638

Fig. 12

13/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA3c

ACTGATGGAT GTCGCCGGAG GCGAGGGGCC TTATCTGATG CTCGGCTGCC TGTTGCTGAT 60
GTGCGCGGCG ATTGGGCTGT TTATCTCAA CACCGCCACG GCGGTGCTGA TGGCGCCTAT 120
TGCCTTAGCG GCGGCGAAGT CAATGGGCGT CTGACCCTAT CCTTTGCCA TGGTGGTGCC 180
GATGGCGGCT TCGGCGGCGT TTATGACCCG GGTCTCCTCG CCGGTAAACA CCCTGGTGCT 240
TGGCCCTGGC AAGTACTCAT TTAGCGATTT TGTCAAAATA GCGGTG 286

Fig. 13

14/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B9CG1

AG CAGCCCCTTC TTCTCAATTT CATCTGTCAC TACCCTGGTG TAGTATCTCA 60
CA TTTTATAGC CTCCTCCCTG GTCTGCTTTT TGATTTTCCT GCCTGTAATC 120
AC ATAAGTGCAA GTAAACATTT CTAAAGTGTG GTTATGCTCA TGTCACTCCT 180
AA ATAGTTTCCA TTACCGTCTT AATAAAATTC GGATTTGTTC TTTCCTATTN 240
CA CCTATGACCG AA 262

Fig. 14

15/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B9CG3

AG CAAAGCCAGT GGTGGAGCT CTCTACTGTG TAAACTCCTA AACCAAGGCC 60
TA AATGGTGGCA GGATTTTAT TATAACATG TACCATGCA AATTCCTAT 120
GA TATATTCTTC TACATTTAAA CAATAAAAT AATCTATTTT TAAAAGCCTA 180
AG TTAGGTAAGA GTGTTTAATG AGAGGGTATA AGGTATAAAT CACCAGTCAA 240
TG CCTATGACCG A 261

Fig. 15

16/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B2CA2

GG GCATGGACGC AGACGCCTGA CGTTTGGCTG AAAATCTTTC ATTGATTCTG 60
AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTNTGTT 120
GG ANAAGGCAAN GAGCTCTTCA GACTATTGGN ATTNTCGTTC GGTCTTCTGC 180
CG NCTTGCNANG ATCTTCAT 208

Fig. 16

17/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA1

GG GCATGGACGC AGACGCCTGA CGTTTGGCTG AAAATCTTTC ATTGATTCTG 60

AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTNTGTT 120

GG ANAAGGCAAN GAGCTCTTCA GACTATTGGN ATTNTCGTTC GGTCTTCTGC 180

CG NCTTGCNANG ATCTTCAT 208

Fig. 17

18/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA2

GG GCATGGACGC AGACGCCTGA CGTITGGCTG AAAATCTTTC ATTGATTCGT 60
AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTNTGTT 120
GG ANAAGGCAAN GAGCTCTTCA GACTATTGGN ATTNTCGTTC GGTCTTCTGC 180
CG NCTTGCNANG ATCTTCAT 208

Fig. 18

19/25

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA3

AG GGAGCAAGGA GAAGGCATGG AGAGGCTCAN GCTGGTCCTG GCCTACGACT 60
CT GTCGCCGGGG ATGGTGGAGA ACTGAAGCGG GACCTCCTCG AGGTCCTCCG 120
TC NCCGTCCAGG AGGAGGGTCT TTCCGTGGTC TNGGAGGAGC GGGGGGAGAA 180
TC ATGGTCNACA TCCCAT TTTTATATAT TATATCTCT TAGGAGGAG 204

Fig. 19

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B4CA1

TC AGGAGCGGGT AGAGTGGAC CATTGAGGGG ATATTCAAAA ATATTATTTT	60
TG ATAGTTGC	TATTGG AGTTTATTTT 120
CC AATCGCAT	T NCTATTTTTA 180
GA TTTGAGA	GTGAGTTTG 240
GC TTAGTATCG	264

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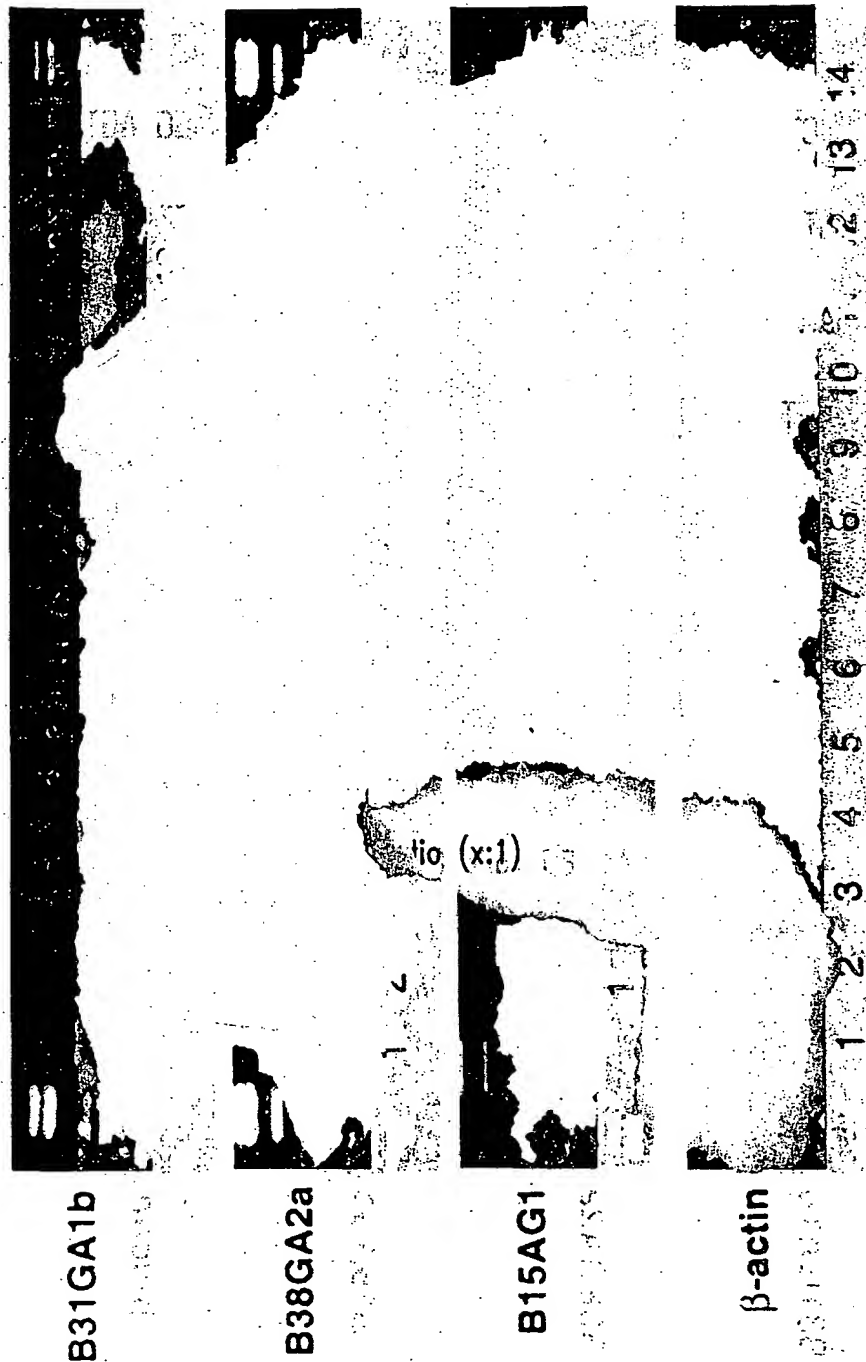
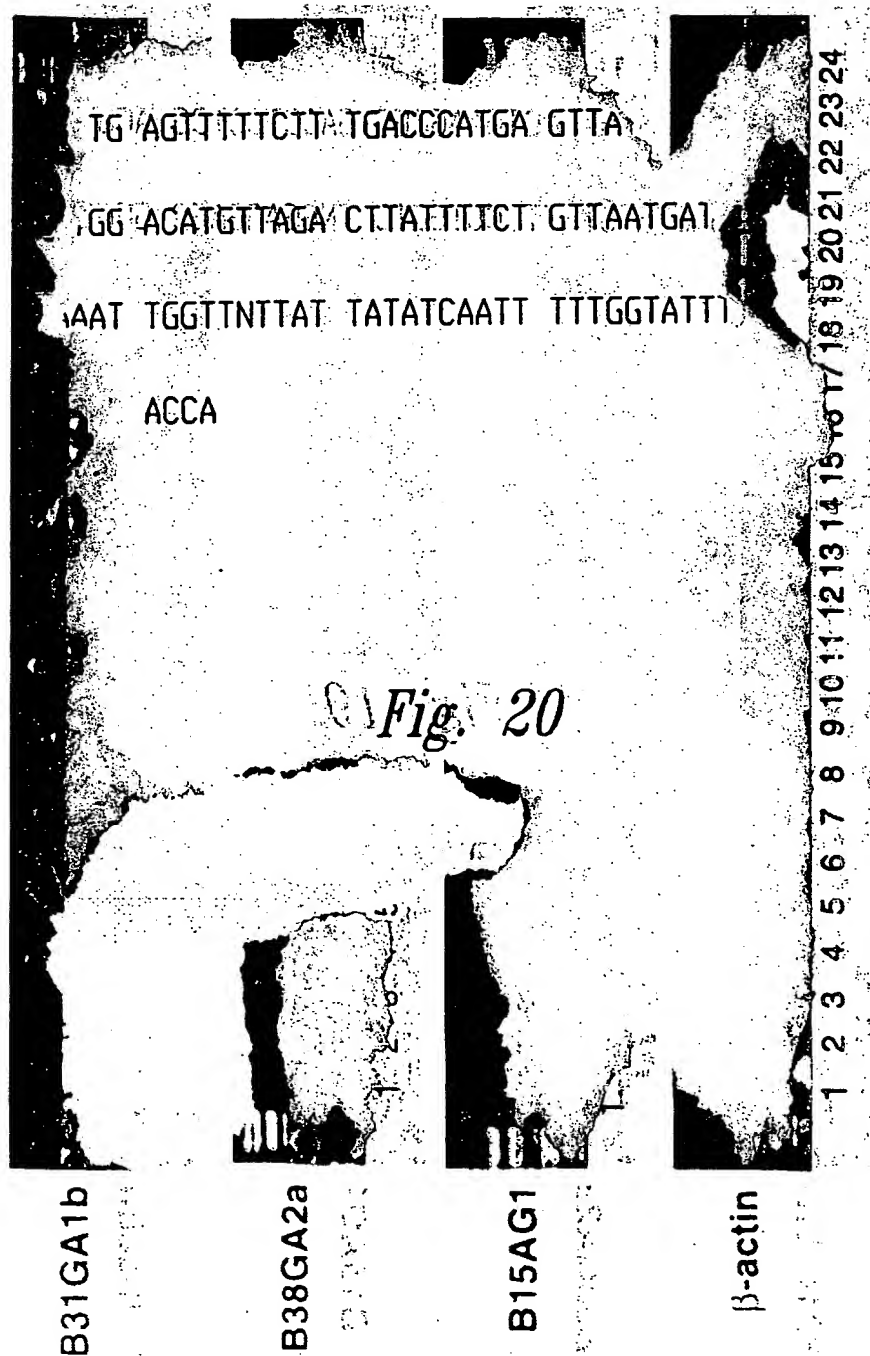


Fig. 21A

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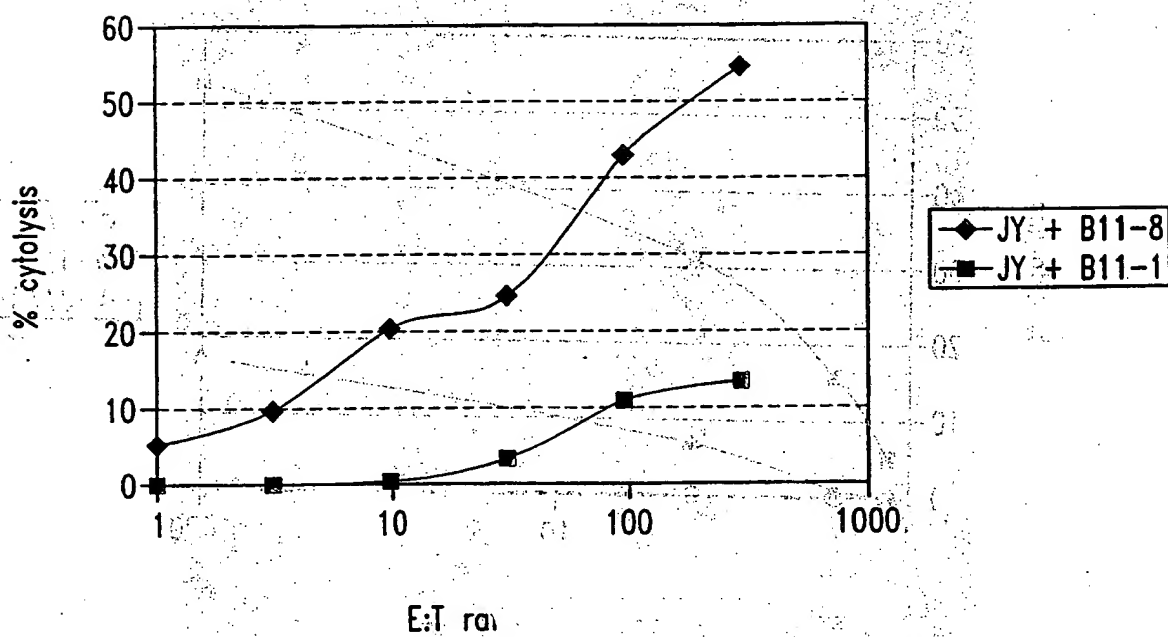
Recognition of Peptide by D142 anti-B11-8
CTL line

Fig. 22

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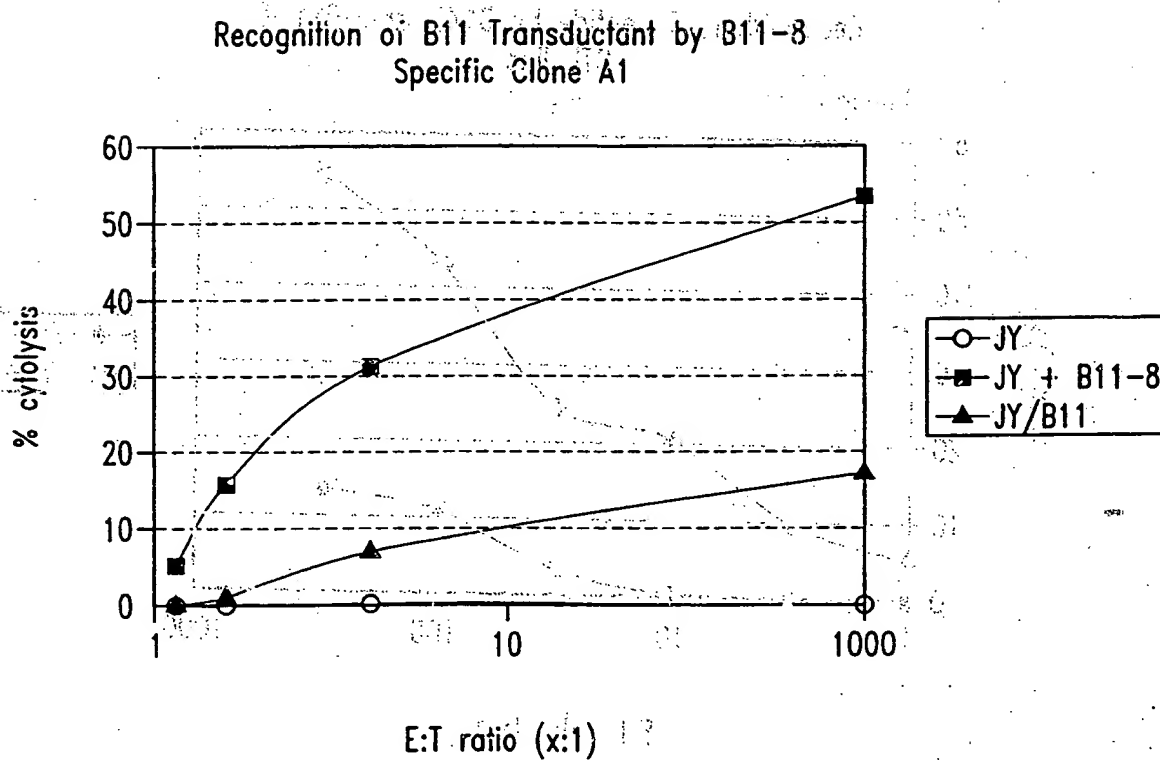


Fig. 23

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Recognition of Tumor Cell Lines by Clone A1

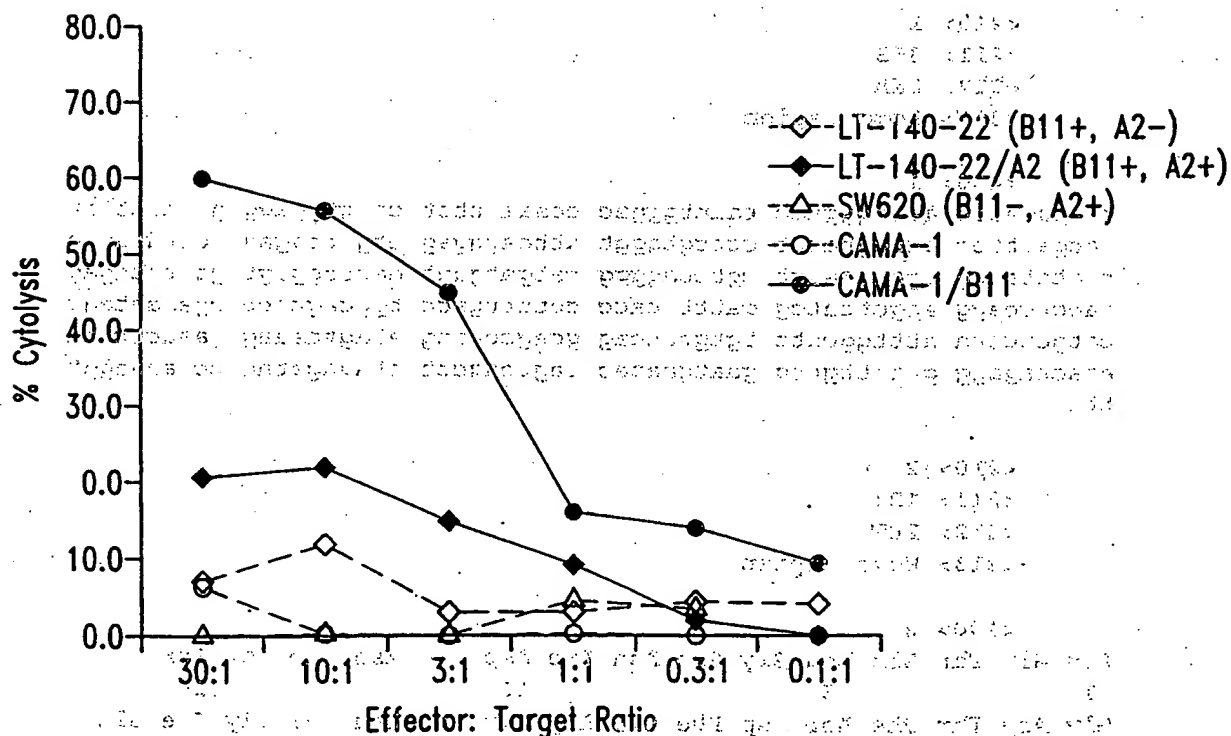


Fig. 24

SEQUENCE LISTING

<110> Corixa Corporation

<120> COMPOSITIONS AND METHODS FOR THE
TREATMENT AND DIAGNOSIS OF BREAST CANCER

<130> 210121.41926PC

<140> PCT

<141> 2000-04-07

<160> 317

<170> FastSEQ for Windows Version 5.0

<210> 1

<211> 363

<212> DNA

<213> Homo sapien

<400> 1

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ttgtctaagg cgattgaagt cgtccagggg catgatgagt caccaggagt gtttttagag	180
cacctccagg aggcctatcg gatttacacc ccttttgacc tggcagcccc cgaaaatagc	240
catgctctta atttggcatt tgtggctcag gcagcccag atagtaaaag gaaactccaa	300
aaactagagg gattttgctg gaatgaatac cagtcagctt ttagagatag cctaaaaggt	360
ttt	363

<210> 2

<211> 121

<212> PRT

<213> Homo sapien

<400> 2

Leu Glu Thr Gln Leu Gly Pro Asn Trp Asp Pro Asn Phe Ser Ser Gly	
1 5 10 15	
Gly Arg Thr Phe Asp Asp Phe His Arg Tyr Leu Leu Val Gly Ile Gln	
20 25 30	
Gly Ala Ala Gln Lys Pro Ile Asn Leu Ser Lys Ala Ile Glu Val Val	
35 40 45	
Gln Gly His Asp Glu Ser Pro Gly Val Phe Leu Glu His Leu Gln Glu	
50 55 60	
Ala Tyr Arg Ile Tyr Thr Pro Phe Asp Leu Ala Ala Pro Glu Asn Ser	
65 70 75 80	
His Ala Leu Asn Leu Ala Phe Val Ala Gln Ala Ala Pro Asp Ser Lys	
85 90 95	
Arg Lys Leu Gln Lys Leu Glu Gly Phe Cys Trp Asn Glu Tyr Gln Ser	
100 105 110	
Ala Phe Arg Asp Ser Leu Lys Gly Phe	
115 120	

<210> 3

<211> 1080

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (1080)

<223> n = A,T,C or G

<400> 3

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tcttcaaagc	ctaacagatc	aagcagctct	ccggtgcaca	acctgcgccc	aggtaaattgc	180
caaaaaagg	cctaaaccca	gcccaggcca	ccgtctccaa	gaaaactcac	caggagaaaa	240
gtgggaaatt	gactttacag	aagtaaaacc	acaccgggct	gggtacaaat	accttctagt	300
actggtagac	accttctctg	gatggactga	agcatttgc	acaaaaacg	aaactgtcaa	360
tatggtagtt	aagtttttac	tcaatgaaat	catccctcga	cgtgggctgc	ctgttgccat	420
agggtctgat	aatggaaacg	ccttcgcctt	gtctatagtt	taatcagtc	gtaaggcggt	480
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tgttagtctc	cttcccttag	ccctacttag	agttaagggt	cacccttac	tgggctgggt	660
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gccatttgg	caaaaatttc	ncaactaatt	tntacgtnc	taegtctccc	caacaggtan	780
aaaaatctnc	tgcccttttc	aagggaacat	cccatccatt	cctnaacaaa	aggcctgccn	840
ttcttcccc	agttaaactnt	ttttnttaa	aattcccaaa	aaangaaccn	cctgctggaa	900
aaacncccc	ctccaanccc	cggcnaagn	ggaaggttc	cttgaatccc	nccccnna	960
anggcccgga	accnttaaan	tngttcngg	gggtnggcc	taaaagnccn	atttggtaaa	1020
cctanaaatt	ttttcttttn	taaaaaccac	ntttntttt	ttcttaacaa	aaacctntt	1080

<210> 4

<211> 1087

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (1087)

<223> n = A,T,C or G

<400> 4

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caagtaggcc	ctttaaaacta	ctcacctgtg	ttgtcttcta	atttattctg	ttttattttg	120
tttccatcat	tttaaggggt	taaaatcatc	ttgttcagac	ctcagcatat	aaaatgaccc	180
atctgtagac	ctcaggctcc	aaccataccc	caagagttgt	ctggttttgt	ttaaattact	240
gccaggtttc	agctgcagat	atccctggaa	ggaatattcc	agattccctg	agtagtttcc	300
agggttaaat	cctataggct	tcttctgttt	tgaggaagag	ttcctgtcag	agaaaaacat	360
gattttggat	ttttaacttt	aatgcttgtg	aaacgctata	aaaaaaattt	tctaccctta	420
gctttaaagt	actgttagtg	agaaattaaa	attccttcag	gaggattaaa	ctgccatttc	480
agttacccta	attccaaatg	ttttgggtgt	tagaatcttc	tttaatgttc	ttgaagaagt	540
gttttatatt	ttcccatcna	gataaattct	ctcncncctt	ntttntntnt	ctntttttt	600
aaaacggant	cttgcctcgt	tgtccangct	gggaattttt	ttttggccaa	tctccgctnc	660
cttgcaanaa	tntgcntec	caaaattacc	ncctttttcc	cacctccacc	ccnnggaatt	720
acctggaatt	anaggccccc	ncccccccc	cggctaattt	gtttttgttt	ttagtaaaaa	780
acgggtttcc	tgtttttagt	aggatggccc	anntctgacc	ccntnatcnt	ccccctngc	840
cctcnaatnt	tnggnntang	gcttaccccc	cccnngnngt	tttctcccat	tnaaattttc	900

tntggantct tgaatnncgg gttttccett ttaaaccnat ttttttttth nnnccccan 960
ttttnccetcc ccctntnta anggggggtt cccaanccgg gtcncccc angtecccaa 1020
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cnantnt 1087

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<211> 1010
<212> DNA
<213> Homo sapien

<220>
<221> misc feature
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<223> n = A,T,C or G

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aggtaacaca catactatct cccaataacc taccacaag ctcaacaatt ttaaactggt 180
aggatcactg gctctaatec ccatgacatg aggtcaccac caaaccatca agcgctaaac 240
agacagaatg tttccactcc tgatccactg tgtgggaaga agcaccgaac ttaccactg 300
gggggctgc ntcanaanaa aagcccatgc cccgggtnt ncttttnaac cggaacgaat 360
naaccacca tccccacac tctctgttc ntgggcccctg catcttggtg cctcntntnc 420
tttnggggan acntggggaa ggtacccat ttenttgacc ccnanaaaa acccngtgg 480
cccttgccc tgattcnct gggccttttc tcttttccct tttgggtgt ttaaattccc 540
aatgtcccn gaacctctc cntnctgec aaaacctacc taaattntc nctangmntt 600
ttcttgggt tnttttcaa aggtnaect nctgttcn nccnacnaa aattnttcc 660
ntatnntgn cccnaaaaa nnnatcnnc cnaattgcc gaattggtt ggttttccct 720
nctggggaa accctttaa tttccccct ggccggcccc cctttttcc ccccttnga 780
aggcaggngg ttcttccga acttccaatt ncaacagecn tgccattgn tgaaccctt 840
ttcetaaat taaaaaatan ccggttnngg nnggcctett tcccctcng gngggngng 900
aaantcetta cccnaaaaa ggttgcttag ccccngtcc cactcctcc nggaaaaatn 960
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<210> 6
<211> 950
<212> DNA
<213> Homo sapien

<220>
<221> misc feature
<222> (1)...(950)
<223> n = A,T,C or G

<400> 6

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ctgggattac aggcgtgcaa caccacaccc ggctaatttt gtatttttaa tagagatggg 180
gttttccct gttggccan atggtctcna acccctgacc tcnngtgatc ccccnbccn 240
ngantcma ctgctgggga tnnccgnnn nnnctcccn ncnnnnnnn ncnnttccn 300
tntccttnc tnnnnnnnn cntctntcc ncttctcnc cnnntntnt cnnnnccnn 360
cnnccnct nccnnnnnt tcnctnncn tntcnnncn nntcnnncn cnnnnctnn 420
cnnctacnt nnnnnnnnt cntctntnn cctcnnncn cctcnnncn tntctctcn 480
ntnnnnnct cnnnnntct cntcnnncn tncctcnnn ncnncctcc nctcncnc 540
ctntttttn cnnnnntcc ntncctttn nntcnnntn cnnctcncn ncnnttntc 600

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cncncnnttc cttncnntn nnnntncnnn cncntcnntc ntttntctct nnnceccnnc 660
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tntcnnttc ntcnntnnt tncntcnnc nncnntncnc tncntntnt ctnnntcnnc 780
tcnntntcn cncntntn ctntctctn tntctctccc ctncctnct ctttncncc 840
ccnntntntn tnnncnnt nctnnnncnc cttntttcn tctctnctnn nntnnccctc 900
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<210> 7

<211> 1086

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

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<223> n = A,T,C or G

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agaaaaatc ttctgccttg agatgctgtt aatctgtaac cctagcccca accctgtgct 180
cacagagaca tgtgtgtgtg tgactcaagg ttcaatggat ttagggctat gctttgttaa 240
aaaagtgtt gaagataata tgcttgtaa aagtcacac cattctctaa tctcaagtac 300
ccagggacac aatacactgc ggaaggccgc agggacctct gtctaggaaa gccaggatt 360
gtccaagatt tctcccatg tgatagcctg agatattggc tcatgggaag ggtaagacct 420
gactgtcccc cagcccgaca tccccagcc cgacatcccc cagcccgaca cccgaaaagg 480
gtctgtgtcg aggaagatta ntaaaaggagg aaggctctt gcattgaagt aagaagaagg 540
ctctgtctcc tgctgtctcc tgggcaataa aatgtcttgg tgtaaaacc gaatgtatgt 600
tctacttact gagaatagga gaaaacatcc ttagggctgg aggtgagaca cctggcggc 660
atactgtctt ttaatgcacg agatgtttgt ntaattgcca tccagggcc ncccccttcc 720
ttaactttt atganacaaa aactttgtc ncttttctg cgaacctct cccctattan 780
cctattggcc tgcccatccc ctccccaan ggtgaaaana tgctntaaa tncgagggaa 840
tccaaaacnt ttcccggtg gtcccttcc caaccctgc cctgggcnn ttccctccc 900
aacntgtccc ggntccttcn ttccncccc cttccngan aaaaaacccc gnttganggn 960
gccccctcaa attataacct ttccnaaaca aarmggtcn aagggtggtt gnttcgggtg 1020
cgggtggcct tgagggtccc cctncccc aatttgaan cngtntttt ttattgccc 1080
ntcccc 1086

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<210> 8

<211> 1177

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1)... (1177)

<223> n = A,T,C or G

<400> 8

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atggtgttta aatccagcta cactacttcc tgactcaaac tccactatc ctgttcata 180
ctgtcaggaa ctgttgaaa ctactgaaac tggccgacct gatcttcaa atgtgccct 240
aggaaagggt gatgccacc tggtcacaga cagtaccncc ttctcgaga agggactacg 300
aggggcccgt gcanctgtta ccaaggagac tnatgtgtt tgggtcagg ctttaccanc 360

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aaacacctca ncnncnaagg ctgaattgat cgccctcact caggetctcg gatggggtaa 420
gggatattaa cgtaaacact gacagcaggt acgcctttgc tactgtgcat gtacgtggag 480
ccatctacca ggagcgtggg ctactcactc ggcaggtggc tgtnatccac tgtaaangga 540
catcaaaagg aaaacnnggc tgggtcccggt ggtaaccana aanctgatch ncagctcnaa 600
gatgctgtgt tgactttcac tcnncctct taaacttgct gccacacntc tcctttccca 660
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accaataaaa acgggggangg tnggtnganc nncctgaccc aaaaataatg gatcccccg 780
gctgcaggaa ttcaattcan ccttatcnat acccccaacn ngnggggggg ggcngtnc 840
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gnggnnaggc cntcacccc cttntgtng gngggnc 1177

<210> 9

<211> 1146

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1) (1146)

<223> n = A,T,C or G

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agactccatc agtgaggtca aagcctgggg cttttcagag aaggaggat tatgggtttt 180
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catcacccag agggacttgt gctctctca gtgtagtag aggggtact tcctccacc 300
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atggaagggt tgctcctgac caaactcagc cattgatcaa tgtagggaa actgatcagg 600
gaagccggga atttcattaa caaccgcca cacagcttga acattgtgag gttcagtga 660
ccttcaaggg gccactccac tccaacttg gccattctac tttgnaaat tccaaaact 720
tcctttttta aggcgaate cntantccct naaaaacnaa aaaaatctg cncctattct 780
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cntttnttaa attgaacctn aattcnccc cccaaaaaa aaccncng gggggcggat 900
ttccaaaaac naattccctt accaaaaaac aaaaaccnc cctnttccc ttcnccctn 960
ttcttttaat tagggagaga tnaagcccc caatttcng gnetngatnn gtttcccccc 1020
ccccatttt cnaaacttt tcccanca ggaancnc cttttttng gtengattna 1080
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<211> 545

<212> DNA

<213> Homo sapien

<400> 10

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tattggctct gagttctgag gccagttttc ttcttctgtt gagtatgcgg gattgtcagg 180
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 ggtagatggc tccacgtaca tgcacagtag caaaggcgta cctgctgtca gtgttaacgt 420
 taatatcctt accccatcgg agagcctgag tgaggcgat caattcagcc cttttgtgct 480
 gaggtgtttg ctggttaagc cctgaacca caacacatct gtctccatgg taacagctgc 540
 accgg 545

<210> 11
 <211> 196
 <212> DNA
 <213> Homo sapien
 <400> 11
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 ggggggatcg cttgagccca agatttcaag actagtctgg gtaacatagt gagaccctat 120
 ctctacgaaa aaataaaaaa atgagcctgg tgtagtggca cacaccagct gaggagggag 180
 aatcgagcct aggaga 196

<210> 12
 <211> 388
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
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 <223> n = A,T,C or G

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 aataaaataa ggaaaacgat gtctgtgtat agccaagtca gntatcctaa aaggagatac 180
 taagtacat taaatatcag aatgtaaaac ctgggaacca ggttcccagc ctgggattaa 240
 actgacagca agaagactga acagtactac tgtgaaaagc ccgaagnggc aatatgttca 300
 ctctaccgtt gaaggatggc tgggagaatg aatgctctgt cccccagtcg caagctcact 360
 tactatacct cttttatagc ctaggaga 388

<210> 13
 <211> 337
 <212> DNA
 <213> Homo sapien

<400> 13
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 acaagatatg atttctacat cagatgtctt ttcttttctt gtttatttcc tttttatttc 180
 ggttgtgggg tgaatgtaa tagctttgtt tcaagagaga gttttggcag tttctgtagc 240
 ttctgacact gctcatgtct ccaggcatct atttgcactt taggaggtgt cgtgggagac 300
 tgagaggtct attttttcca tatttgggca actacta 337

<210> 14
 <211> 571
 <212> DNA

<213> Homo sapien
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 <222> (1) ... (571)
 <223> n = A,T,C or G
 <400> 14

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aaaatcatat	tccatatttt	acgctcgagg	gtttttacog	gttccttttt	acactcctta	180
aaacagtttt	taagtcgttt	ggaacaagat	atTTTTtctt	tcctggcagc	ttttaacatt	240
atagcaaatt	tgtgtctggg	ggactgctgg	tcactgtttc	tcacagtgtg	aatcaaggc	300
atttgaacc	aagaaaaaaa	aatttttttg	ttttatttga	aactggaccg	gataaacggt	360
gtttggagcg	gctgctgtat	atagttttaa	atgggtttatt	gcacctcctt	aagttgcact	420
tatgtggggg	ggggnttttg	natagaaagt	ntttantcac	anagtcacag	ggacttttnt	480
cttttggnna	ctgagctaaa	aagggtgnt	tttcgggtgg	gggcagatga	aggtcacag	540
gaggcctttc	tcttagaggg	gggaacttct	a			571

<210> 15
 <211> 548
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (548)
 <223> n = A,T,C or G

<400> 15

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tccccacccc	gcactgaaac	ttcaccttct	aactgtctac	ctaaccaaat	tctacccttc	180
aagtcttttg	tgctgtctca	ctactctttt	tttttttttt	ttnttttttg	agatggagtc	240
tggtgtgtgc	gcccaggggt	ggagtacaat	ggcacaacct	cagctcactg	naacctccgc	300
ctcccaggtt	catgagattc	tcctgnttca	gccttcccag	tagctgggac	tacagggtgtg	360
catcaecatg	cctggntaat	cttttttngt	tttngggtag	agatgggggt	tttatatgtt	420
ggccaggntg	gtntcgaact	cctgacctca	agtatccac	ccacctcagg	ctcccaaagt	480
gctaggatta	cagacatgag	ccactgngcc	cagncctggt	gcattgtcac	ttctctaggc	540
aactacta						548

<210> 16
 <211> 638
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (638)
 <223> n = A,T,C or G

<400> 16

ttccgttatg	cacatgcaga	atattctatc	ggtacttcag	ctattactca	ttttgatggc	60
gcaatccgag	cctatcctca	agatgagtat	ttagaaagaa	ttgatttagc	gatagaccaa	120
gctggtaagc	actctgacta	cacgaaattg	ttcagatgtg	atggatttat	gacagttgat	180

```

ctttggaaga gattattaag tgattattht aaaggggaatc cattaattcc agaatatctt 240
ggtttagctc aagatgatat agaaatagaa cagaaagaga ctacaaatga agatgtatca 300
ccaactgata ttgaagagcc tatagtagaa aatgaattag ctgcatttat tagccttaca 360
catagcgatt ttctgatga atcttatatt cagccatcga catagcatta cctgatgggc 420
aaccttacga ataatagaaa ctgggtgcgg ggctattgat gaattcatcc ncagtaaatt 480
tggatatnac aaaatataac tggattgcat ttggatgatg gaatactaaa tctggcaaaa 540
gtaactttgg agctactagt aacctctctt tttgagatgc aaaattttct tttaggggtt 600
cttattctct actttacgga tattggagca taacggga 638

```

<210> 17

<211> 286

<212> DNA

<213> Homo sapien

<400> 17

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actgatggat gtgcgcggag ggcagggggcc ttatctgatg ctgcggctgcc tggctcgtgat 60
gtgcgcggcg attgggctgt ttatctcaaa caccgccacg gcggtgctga tggcgccat 120
tgccttagcg gcggcgaagt caatgggcgt ctaccctat ccttttgcca tgggtggggc 180
gatggcggtc tggcgggcgt ttatgacccc ggtctcctcg ccggttaaca ccctgggtgt 240
tggccctggc aagtactcat ttagcgattt tgtcaaaata ggcgtg 286

```

<210> 18

<211> 262

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (262)

<223> n = A, T, C or G

<400> 18

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tcggatcatg cagcccttc ttctcaattt catctgtcac taccctgggtg tagtatctca 60
tagccttaca tttttatagc ctctccctg gtctgtcttt tgattttcct gcctgtaatc 120
catatcacac ataactgaa gtaaacattt cttaaagtgtg gttatgctca tgtcactcct 180
gtgncaagaa atagtttcca ttaccgtctt aataaaattc ggatttggtc ttttctattn 240
tcactcttca cctatgaccg aa 262

```

<210> 19

<211> 261

<212> DNA

<213> Homo sapien

<400> 19

```

tcggatcatg caaagccagt ggtttgagct ctctactgtg taaactccta aaccaaggcc 60
atztatgata aatgggtggc ggatttttat tataaacatg taccatgca aatttcctat 120
aactctgaga tatattcttc tacatttaaa caataaaaat aatctatttt taaaagccta 180
atgtgcgtag ttaggtaaga gtgtttaatg agagggtata aggtataaat caccagtcaa 240
cgtttctctg cctatgaccg a 261

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<210> 20

<211> 294

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (294)

<223> n = A,T,C or G

<400> 20

tacaacgagg	cgacgtcggg	aaaatcggac	atyaagccac	cgctgggtctt	ttcgtccgag	60
cgataggcgc	cggccagcca	gcggaacggg	tgcccggaat	gcgaagcgag	cgggagttct	120
tccgactgag	tatgaatctt	gttgtgaaaa	tactcgcgc	cttcgttcga	cgacgtcgcg	180
tcgaaatctt	cgantcctt	acgatcgaag	tcttcgtggg	cgacgatcgc	ggtcagttcc	240
gccccaccga	aatcatgggt	gagccggatg	ctgnccccga	agnctcgtt	tgtn	294

<210> 21

<211> 208

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (208)

<223> n = A,T,C or G

<400> 21

ttggtaaagg	gcatggacgc	agacgcctga	cgtttggtcg	aaaatctttc	attgattcgt	60
atcaatgaat	aggaaaattc	ccaaagaggg	aatgtcctgt	tgctcgccag	ttttctngtt	120
gttctcatgg	anaaggcaan	gagctcttca	gactattggn	attntcgttc	ggtcttctgc	180
caactagtcg	ncttgcnang	atcttcat				208

<210> 22

<211> 287

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (287)

<223> n = A,T,C or G

<400> 22

nccnttgagc	tgagtgattg	agatntgtaa	tggttgtaag	ggtgattcag	gcggattagg	60
gtggcgggtc	accgcgcagt	gggtctcccg	acaggccagc	aggatttggg	gcaggtaagg	120
ngtgcgcac	gctcgactat	atgctatggc	aggcgagccg	tggaaggagg	atcagggtcac	180
ggcgctggag	ctttccacgg	tccatgnatt	gngatggctg	ttctaggcgg	ctgttgccaa	240
gcgtgatggg	acgtgggctg	gagcattgat	ttctgggtgcc	aaggtgg		287

<210> 23

<211> 204

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (204)

<223> n = A,T,C or G

<400> 23

ttgggttaaag ggagcaagga gaaggcatgg agaggctcan gctggctctg gcctacgact 60
 gggccaagct ctgcgcgggg atggtggaga actgaagcgg gacctctcg aggtcctccg 120
 ncgttacttc nccgtccagg aggagggtct ttccgtgggtc tnggaggagc ggggggagaa 180
 gatnctcttc atggtcnaca tccc 204

<210> 24

<211> 264

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (264)

<223> n = A,T,C or G

<400> 24

tggattgggtc aggagcgggt agagtggcac cattgagcgg atattcaaaa atattatattt 60
 gtcctaaatg atagtgtctg agtttttctt tgacccatga gttatattgg agtttatttt 120
 ttaactttcc aatcgcatgg acatgttaga cttattttct gttaatgatt nctattttta 180
 ttaaattgga ttgagaaat tggtnnttat tatatcaatt tttggtattt gttgagtttg 240
 acattatagc ttagtatgtg acca 264

<210> 25

<211> 376

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (376)

<223> n = A,T,C or G

<400> 25

ttacaacgag gggaaactcc gtctctacaa aaattaaaaa attagccagg tgtggtgggtg 60
 tgcacccgca atcccagcta cttgggaggt tgagacacaa gantcaccta natgtgggag 120
 gtcaagggtg catgagtcac gattgtgcca ctgcactcca gcctgggtga cagaccgaga 180
 ccctgcctca anaganaang aataggaagt tcagaaatcn tggntgtggn gccagcaat 240
 ctgcatctat ncaaccctg caggcaangc tgatgcagcc tangttcaag agctgctgtt 300
 tctggaggca gcagtnggg cttccatcca gtatcacggc cacactcgca cnagccatct 360
 gtccctccgtn tgnac 376

<210> 26

<211> 372

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (372)

<223> n = A,T,C or G

<400> 26

ttacaacgag gggaaactcc gtctctacaa aaattaaaaa attagccagg tgtggtgggtg 60
 tgcacctgta atcccagcta cttgggcggc tgagacacaa gaaccaccta aatgtgggag 120

ggccaaggtt gcatgagtca tgatcgcgcc actgcactcc agcctgggtg acagactgag 180
accctgcctc aaaagaaaaa gaataggaag ttccagaaacc ctgggtgtgg ngcccagcaa 240
tctgcattta aacaatecct gcaggcaatg ctgatgcagc ctaagtcca gagctgctgt 300
tctggaggca gnagtaaggg cttccatcca gcatcacggn caacactgca aaagcacctg 360
tcctcgttgg ta 372

<210> 27
<211> 477
<212> DNA
<213> Homo sapien

<400> 27
ttctgtccac atctacaagt tttatttatt ttgtgggttt tcaggggtgac taagtttttc 60
cctacattga aaagagaagt tgctaaaagg tgcacaggaa atcatttttt taagtgaata 120
tgataatatg ggtccgtgct taatacaact gagacatatt tgttctctgt ttttttagag 180
tcacctctta aagtccaatc ccacaatggt gaaaaaaaaa tagaaagtat ttgttctacc 240
ttaaaggaga ctgcagggat tctccttgaa aacggagat ggaatcaatc ttaaataaat 300
atgaaattgg ttgtcttct gggataagaa attcccaact cagtgtgctg aaattcacct 360
gacttttttt gggaaaaaat agtcgaaaat gtcaatttgg tcataaaaat acatgttact 420
attaaaagat atttaaagac aaattccttc agagctctaa gattggtgtg gacagaa 477

<210> 28
<211> 438
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (438)
<223> n = A,T,C or G

<400> 28
tctncaacct ctgtantgtc aaaaaccttn taggctatct ctaaaagctg actggtattc 60
attccagcaa aatccctcta gtttttggag ttccctttta ctatctgggg ctgectgagc 120
cacaaatgcc aaattaagag catggctatt ttccgggggt gacaggcca aaggggtgta 180
aatccgataa gcttcctgga ggtgctctaa aaacactoct ggtgactcat catgcccctg 240
gacgacttca atcgncttag acaagttaat aggtttcttg gcagctccct gaatacccac 300
gaggagatac cggtaggaat cgtcaaaagt tctcctcca cttgagaaat ttgggtccca 360
attagggtccc aattgggtct ctaatcacta ttctcttagc ttctcctcc ggnctattgg 420
ttgatgtgag gttgaaga 438

<210> 29
<211> 620
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (620)
<223> n = A,T,C or G

<400> 29
aagagggtac cagccccaag ccttgacaac ttccataggg tgtcaagcct gtgggtgcac 60
agaagtcaaa aattgagttt tgggatcctc agcctagatt tcagaggata taaagaaaca 120
cctaacacct agatattcag acaaaagttt actacaggga tgaagcttcc acggaaaacc 180

tctactagga aagtacagaa gagaaatgtg ggtttggagc ccccaaacag aatccccctct 240
 agaacactgc ctaatgaaac tgtgagaaga tggccactgt catccagaca ccagaatgat 300
 agaccacca aaaacttatg ccatattgcc tataaaacct acagacactc aatgccagcc 360
 ccatgaaaaa aaaactgaga agaagactgt nccctacaat gccaccggag cagaactgcc 420
 ccaggccatg gaagcacagc ttttatatca atgtgacctg gatgttgaga catggaatcc 480
 nangaaatcn ttttaanact tccacggttn aatgactgcc ctattanatt cngaacttan 540
 atcnggcct gtgacctctt tggtttgccc attccccctt tttggaatgg ctnttttttt 600
 cccatgcttg tncctcttta 620

<210> 30

<211> 100

<212> DNA

<213> Homo sapien

<400> 30

ttacaacgag ggggtcaatg tcataaatgt cacaataaaa caatctcttc tttttttttt 60
 tttttttttt tttttttttt tttttttttt tttttttttt 100

<210> 31

<211> 762

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(762)

<223> n = A,T,C or G

<400> 31

tagtctatgc gccggacaga gcagaattaa attggaagtt gccctccgga ctttctaccc 60
 acactcttcc tgaaaagaga aagaaaagag gcaggaaaga ggtaggatt tcattttcaa 120
 gagtcagcta attaggagag cagagttag acagcagtag gcaccccatg atacaaacca 180
 tggacaaagt ccctgttttag taactgccag acatgatcct gctcaggttt tgaaatctct 240
 ctgcccataa aagatggaga gcaggagtgc catccacatc aacacgtgtc caagaaagag 300
 tctcagggag acaagggtat caaaaaacaa gattcttaat gggaaggaaa tcaaaccaaa 360
 aaattagatt tttctctaca tatatataat atacagatat ttaacacatt attccagagg 420
 tggctccagt ccttggggct tgagagatgg tgaaaacttt tgttccacat taacttctgc 480
 tctcaaattc tgaagtatat cagaatggga caggcaatgt tttgctccac actggggcac 540
 agacccaaat ggttctgtgc ccgaagaaga gaagcccgaa agacatgaag gatgcttaag 600
 ggggggttggg aaagcccaat tgggtantatc ttttctctct gcctgtgttc cngaagtctc 660
 cnctgaagga attcttaaaa ccctttgtga ggaaatgcc ccttaccatg acaantggtc 720
 ccattgcttt tagggngatg gaaacaccaa gggttttgat cc 762

<210> 32

<211> 276

<212> DNA

<213> Homo sapien

<400> 32

tagtctatgc gtgtattaac ctccccctcc tcagtaacaa ccaaagaggc aggagctggt 60
 attaccaacc ccattttaca gatgcacaa taatgacaga gaagtgaagt gacttgcgca 120
 cacaaccagt aaattggcag agtcagattt gaatccatgg agtctgggtc gcactttcaa 180
 tcaccgaata ccctttctaa gaaacgtgtg ctgaatgagt gcatggataa atcagtgtct 240
 actcaacatc tttgcctaga tatcccgcat agacta 276

<210> 33
<211> 477
<212> DNA
<213> Homo sapien
<400> 33
tagtagttgc caaatatttg aaaatttacc cagaagtgat tgaaaacttt ttggaaacaa 60
aaacaaataa agccaaaagg taaaataaaa atatctttgc actctcgta ttacctatcc 120
ataacttttt caccgtaagc tctctgctt gttagtgtag tgtggttata ttaacttttt 180
tagttattat tttttattca cttttccact agaaagtcac tattgattta gcacacatgt 240
tgatctcatt tcattttttc tttttatagg caaaatttga tgctatgcaa caaaaatact 300
caagcccat atcttttttc ccccgaaat ctgaaaattg caggggacag aggggaagtt 360
tcccattaaa aaattgtaaa tatgttcagt ttatgtttta aatgcacaa aacataagaa 420
aattgtgttt acttgagctg ctgattgtaa gcagttttat ctcaggggca actacta 477

<210> 34
<211> 631
<212> DNA
<213> Homo sapien
<400> 34

tagtagttgc caattcagat gatcagaaat gctgctttcc tcagcattgt cttgttaaac 60
cgcatgccat ttggaacttt ggcagtgaga agccaaaagg aagaggtgaa tgacatatat 120
atatatatat attcaatgaa agtaaaatgt atatgtcat atactttcta gttatcagaa 180
tgagttaagc tttatgccat tgggctgctg catattttta tcagaagata aaagaaaaatc 240
tgggcatttt tagaatgtga tacatgtttt tttaaaactg ttaaataatta tttcgatatt 300
tgtctaagaa ccggaatgtt cttaaaattt actaaaacag tattgtttga ggaagagaaa 360
actgtactgt ttgccattat tacagtcgta caagtgcacg tcaagtcacc cactctctca 420
ggcactcagta tccacctcat agctttacac attttgacgg ggaatattgc agcatcctca 480
ggctgacat ctgggaaagg ctgagatcca cctactgtc cttgctcgtt gatttgtttt 540
aaaatatgtt gcttggtgtc acttttaagc cacagccctg cctaaaagcc agcagagaa 600
agaaccgca ccattctata ggcaactact a 631

<210> 35
<211> 578
<212> DNA
<213> Homo sapien
<400> 35

tagtagttgc catcccatat tacagaaggc tctgtataca tgacttattt ggaagtgate 60
tgttttctct ccaaaccat ttatcgtaat ttcaccagtc ttggatcaat cttggtttcc 120
actgatacca tgaaacctac ttggagcaga cattgcacag ttttctgtgg taaaaactaa 180
aggtttattt gctaagctgt catcttatgc ttagtatttt ttttttacag tggggaattg 240
ctgagattac attttgttat tcattagata ctttgggata acttgacact gtcttctttt 300
tttctgtttt aattgctatc atcatgcttt tgaaacaaga acacattagt cctcaagtat 360
tacataagct tgcttgttac gcttggtggt ttaaaggact atctttggcc tcaggttcac 420
aagaatgggc aaagtgtttc cttatgttct gtagtttcca ataaaagatt gccaggggcc 480
gggtactgtg gctgcactg taatcccagc actttgggaa gctgaggctg gcggatcatg 540
ttagggcagg ttttgaac cagcctgggc aactacta 578

<210> 36
<211> 583
<212> DNA
<213> Homo sapien

<400> 36

tagtagttgc	ctgtaatccc	agcaactcag	gaggctgggg	caggagaatc	agttgaacct	60
gggaggcaga	agttgtaatt	agcaaagatc	gcaccattgc	acttcagcct	gggcaacaag	120
agtgagattc	catctcaaaa	acaaaaaaaa	gaaaaagaaa	agaaaaaggaa	aaaacgtata	180
aaccagcca	aaacaaaatg	atcattcttt	taataagcaa	gactaattta	atgtgtttat	240
ttaatcaaag	cagttgaatc	ttctgagtta	ttggtgaaaa	tacccatgta	gttaatttag	300
ggttcttact	tgggtgaacg	tttgatgttc	acagggtata	aaatgggtta	caaggaaaat	360
gatgcataaa	gaatcttata	aactactaaa	aataaataaa	atataaatgg	atagggtgta	420
tggatggagt	ttttgtgtaa	tttaaaatct	tgaagtcatt	ttggatgctc	attgggtgtc	480
tggtaatttc	cattaggaaa	aggttatgat	atggggaaac	tgtttctgga	aattgcggaa	540
tgtttctcat	ctgtaaaatg	ctagtatctc	agggcaacta	cta		583

<210> 37

<211> 716

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(716)

<223> n = A,T,C or G

<400> 37

gatctactag	tcatntggat	tctatccatg	gcagctaagc	ctttctgaat	ggattctact	60
gctttcttgt	tctttaatcc	agacccttat	atatgtttat	gttcacaggc	agggcaatgt	120
ttagtgaaaa	caattctaaa	ttttttat	tgcattttca	tgctaatttc	cgtcacactc	180
cagcaggctt	cctgggagaa	taaggagaaa	tacagctaaa	gacattgtcc	ctgcttactt	240
acagccta	ggtatgcaa	accacttcaa	taaagtaaca	ggaaaagtac	taaccaggta	300
gaatggacca	aaactgat	agaaaaatca	gaggaagaga	ggaacaaata	tttactgagt	360
cctagaatgt	acaaggcttt	ttaattacat	attttatgta	aggcctgcaa	aaaacagggtg	420
agtaatcaac	atgtgtccca	ttttacatat	aaggaaactg	aagcttaaat	tgaataattt	480
aatgcataga	ttttatagtt	agaccatgtt	cagggtcccta	tggtatactt	actagctgta	540
tgaatatgag	aaaataattt	tggtattttc	ttggcatcag	tattttctac	tgcaaaaataa	600
agctaaagt	attagcaaa	cagtcagcat	agtgcctgat	acatagtagg	tgctccaaac	660
atgattacnc	tantatnngg	tattanaaaa	atccaatata	ggcntggata	aaaccg	716

<210> 38

<211> 688

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(688)

<223> n = A,T,C or G

<400> 38

ttctgtccac	atatcatccc	actttaattg	ttaatcagca	aaactttcaa	tgaaaaatca	60
tccattttta	ccaggatcac	accaggaaac	tgaagggtga	ttttttttta	ccttaaaaaa	120
aaaaaaaaaa	accaaacaaa	cctaaacaga	ttaacagcaa	agagttctaa	aaaatttaca	180
tttctcttac	aactgtcatt	cagagaacaa	tagttcttaa	gtctgttaaa	tcttggcatt	240
aacagagaaa	cttgatgaan	agttgtactt	ggaatattgt	ggattttttt	ttttgtctaa	300
tctcccccta	ttgttttgcc	aacagtaatt	taagtttgtg	tggaacatcc	cogtagttga	360
agtgtaaaca	atgtatagga	aggaatatat	gataagatga	tgcatcacat	atgcattaca	420
tgtagggacc	ttcacaactt	catgcactca	gaaaacatgc	ttgaagagga	ggagaggacy	480

gccacgggtc accatccagg tgccttgagg acagagaatg cagaagtggc actgttgaaa 540
tttagaagac catgtgtgaa tggtttcagg cctgggatgt ttgccaccaa gaagtgcctc 600
cgagaaattt ctttccatt tgggaatacag ggtggccttg tgggtacggg ggttgaccca 660
acgaagaaaa tgaaattctg ccttttcc 688

<210> 39
<211> 585
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (585)
<223> n = A,T,C or G

<400> 39

tagtagttgc cgcnnaccta aaanttggaa agcatgatgt ctaggaaaca tantaaaata 60
gggtatgcct atgtgctaca gagagatggt agcatttaaa gtgcatantt ttatgtattt 120
tgacaaatgc atatnccctc ataateccaca actgattacg aagctattac aattaaaaag 180
tttggccggg cgtggtgggc ggtggctgac gctgtaatc ccagcacttt gggaggccga 240
ggcacgcgga tcacgaggtc gggagttcaa gaccatcctg gctaacacgg tgaaagtcca 300
tctctactaa aaatacgaaa aaattacccc ggctggtggg cgggcgctg tagtcccage 360
tactccggag gctgaggcag gagaatggcg tgaaccagg acacggagct tgcagtgtgc 420
caacatcagc tcactgcctt ccagcctggg ggacaggaac aagantcccg tctctanaaa 480
agaaaaatac tactnatant ttcnacttta ttttaantta cacagaactn cctcttggtg 540
cccccttacc attcatctca cccacctcct atagggcacn nctaa 585

<210> 40
<211> 475
<212> DNA
<213> Homo sapien

<400> 40

tctgtccaca ccaatcttag aagctctgaa aagaatttgt ctttaaatat cttttaatat 60
taacatgtat ttatggacc aaattgacat ttctgactgt tttttccaaa aaagtcaggt 120
gaatttcagc aactgaggtt gggaatttct tatccagaa gaccaacca tttcatattt 180
atttaagatt gattccatac tccgttttca aggagaatcc ctgcagtctc cttaaaggta 240
gaacaaatac ttctattttt tttttcacca ttgtgggatt ggactttaag aggtgactct 300
aaaaaaacag agaacaaata tgtctcagtt gtattaagca cggaccata ttatcatatt 360
cacttaaaaa aatgatttcc tgtgcacett ttggcaactt ctcttttcaa tgtagggaaa 420
aacttagtca cctgaaaac ccacaaaata aataaaactt gtagatgtgg acaga 475

<210> 41
<211> 423
<212> DNA
<213> Homo sapien

<400> 41

taagagggtg catcgggtga gaacgtaggc acatctagag cttagagaag tctggggtag 60
gaaaaaaatc taagtattta taagggtata ggtaacattt aaaagtaggg ctagctgaca 120
ttatttagaa agaacacata cggagagata agggcaaagg actaagacca gaggaacact 180
aatatttagt gatcacttcc attcttggtg aaaatagtaa cttttaagtt agcttcaagg 240
aagatttttg gccatgatta gttgtcaaaa gttagttctc ttgggtttat attactaatt 300
ttgttttaag atccttggtg gtgctttaat aaagtcattt tatatcaaac gctctaaaac 360
attgtagcat gttaaatgct acaatatact taccatttgt tgtatatggc tgtaccctct 420

cta

423

<210> 42
<211> 527
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(527)
<223> n = A,T,C or G

<400> 42

tctcctaggc	taatgtgtgt	gtttctgtaa	aagtaaaaag	ttaaaaattt	taaaaataga	60
aaaaagctta	tagaataaga	atatgaagaa	agaaaatatt	ttgtacatt	tgcaaatga	120
gtttatgttt	taagctaagt	gttattacaa	aagagccaaa	aaggttttta	aaattaaaac	180
gtttgtaaag	ttacagtacc	cttatgttaa	tttataattg	aagaaagaaa	aacttttttt	240
tataaatgta	gtgtagccta	agcatacagt	atttataaag	tctggcagtg	ttcaataatg	300
tcttaggcct	tcacattcac	tactgactc	accagagca	acttccagtc	ctgtaagctc	360
cattcgtggt	aagtgcctta	tacaggtgca	ccatttattt	tacagtattt	ttactgtacc	420
ttctctatgt	ttccatatgt	ttcgatatac	aaataccact	ggttactath	gcccnacagg	480
taattccagt	aacacggcct	gtatacgtct	ggtancccta	gngaaga		527

<210> 43
<211> 331
<212> DNA
<213> Homo sapien

<400> 43

tcttcaacct	cgtaggacaa	ctctcatatg	cctgggcact	atttttaggt	tactaccttg	60
gctgcccttc	tttaagaaaa	aaaaaagaag	aaaaaagaac	ttttccacaa	gtttctcttc	120
ctctagttgg	aaaattagag	aatcatgtt	tttaattttg	tgttatttca	gatcacaaat	180
tcaaacactt	gtaaacatta	agcttctgtt	caatcccttg	ggaagaggat	tcattctgat	240
atttacgggt	caaaagaagt	tgtaatattg	tgcttggaac	acagagaacc	agttattaac	300
ttcctactac	tattatataa	taaataataa	c			331

<210> 44
<211> 592
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(592)
<223> n = A,T,C or G

<400> 44

ggcttagtag	ttgccaggca	aaatacgtt	gattctcttc	aggagccacc	cccaacaccc	60
ctgtttgctt	ctagacctat	acctagacta	aagtcccagc	agacccttag	aggtgaggtt	120
cagagtgacc	cttgaggaga	tgtgctacac	tagaaaagaa	ctgcttgagt	tttctaattt	180
atataagcag	aaatctggag	aagagtcata	ggaatggata	ttaaggggtg	gagataatgg	240
cggaaggaat	atagagttag	atcaggctgg	acttattgat	ttgaaccac	taagtagaga	300
ttctgctttt	gatgttcgag	ctcagggagt	taaaaaaggt	tttaatgggt	ctaatagttt	360
atttgcttgg	ttagctgaaa	tatggataaa	agatggccca	ctgtgagcaa	gctggaaatg	420
cctgatctct	ctcagtttaa	tgtagaggaa	gggatccaaa	agtttaggga	ganttggtg	480

ctggraktgg attggctact ttgrgaccta cccwtcccag ctggggagggt ccagaagata 540
cacccttgac caacgctttg cgaaatggat ttgtgatggc ggcaactact aa 592

<210> 45
<211> 567
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (567)
<223> n = A,T,C or G

<400> 45
ggcttagtag ttgccattgc gagtgccttc tcaacgagcg ttgaacatgg cggattgtct 60
agattcaacg gatttgagtt ttaccagcaa agtgaaccaa gcgcggccca gagaattatg 120
ggttggttgg ctttgaagaag atggaatcc tgtaggccta gtcagaaaag ccttcttgca 180
gaacagttgg ttctcgggcg aacgctcatc aagatgccca ttggaaaggc tagcgtgtat 240
ttgggagagc ctgatagcgt gtcttctgat gatgtttgtg cttggacagt gacaaaagat 300
atgcaaagca agtccgaact agacgtcaag ctctcgtgagc aaattattgt agactcctac 360
ttatactgtg aggaatgata gccaaagggtg gggactttaa gactaagggtg gtttgtactt 420
gcgcgatga tcccaggcag aaagamctga tcgctagttt tatacgggca actactaagc 480
cgaattccag cacactggcg gccgttacta attggatccg anctcggtag cagcttgatg 540
cataccttga gttwtctata ntgtcnc 567

<210> 46
<211> 908
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (908)
<223> n = A,T,C or G

<400> 46
gagcgaaga ccgagggcag ngntangng cgangaagcg gagagggcca aaaagcaacc 60
gctttccccg gggggtgccg attcattaag gcaggtggag gacaggttcc ccgatggaag 120
gcggcagggg cgcaagcaat taatgtgagt aggcattca ttagcaccgg ggcttaacat 180
ttaagcttcg ggttggtatg tgggtgggaat tgtgagcgga taacaatttc acacaggaaa 240
cagctatgac catgattacg ccaagctatt taggtgacat tatagaataa ctcaagttat 300
gcatcaagct tggtagcgag ttccgatcca ctagtaacgg ccgccagtgt gtggaattcg 360
gcttagtagt tgccgaccat ggagtgtctac ctaggctaga atacctgagy tcttccctag 420
cctcactcac attaaattgt atcttttcta cattagatgt cctcagcgcc ttatttctgc 480
tggacwatcg ataaattaat cctgatagga tgatagcagc agattaatta ctgagagtat 540
gttaattgtg catccctcct atataacgta tttgcatttt aatggagcaa ttctggagat 600
aatccctgaa gccaaaggaa tgaatcttga gggtagaaga gccagaatca gtgtccagct 660
gcagttgtgg gagaagggtga tattatgtat gtctcagaag tgacaccata tgggcaacta 720
ctaagccgga attccagcac actggcgggc gttactaatg gatccgagct cggtaaccaag 780
cttgatgcac agcttgagta tctatagtgt cactaaatag cctggcggtta tcatggatcat 840
agctgtttcc tgtgtgaaat tgttatccgc tcccaattcc cccaccata cgagccggaa 900
cataaagt 908

<210> 47
<211> 480

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1)...(480)

<223> n = A,T,C or G

<400> 47

tgccaacaag gaaagtttta aatttcccct tgaggattct tgggtgatcat caaattcagt	60
ggtttttaag gttgttttct gtcaaataac tctaacttta agccaaacag tatatggaag	120
cacagataka atattacaca gataaaagag gagttgatct aaagtaraga tagttggggg	180
ctttaatttc tggaaacctag gtctcccat cttcttctgt gctgaggaaac ttcttggaag	240
cggggattct aaagttcttt ggaagacagt ttgaaaacca ccatgttggt ctcagtacct	300
ttatttttaa aaagtaggtg aacattttga gagagaaaag ggcttggtg agatgaagtc	360
ccccccccc cttttttttt ttttagctga aatagatacc ctatgttnaa rgaarggatt	420
attatttacc atgccaytar scacatgctc ttgatgggc nytccectac cctccttaag	480

<210> 48

<211> 591

<212> DNA

<213> Homo sapien

<400> 48

aagagggtac cgagtggat ttccgcttca ctagtctggt gtggctagtc ggtttcgtgg	60
tggccaacat tacgaacttc caactcaacc gttcttggac gttcaagcgg gagtaccggc	120
gaggatggtg gcgtgaattc tggcctttct ttgccgtggg atcggtagcc gccatcatcg	180
gtatgtttat caagatcttc tttactaacc cgacctctcc gatttacctg ccagagccgt	240
ggtttaacga ggggagggg atccagtcac gcgagtactg gtcccagatc ttgccatcg	300
tcgtgacaat gcctatcaac ttcgctgtca ataagttgtg gacctccga acggtgaagc	360
actccgaaaa cgccgggtgg ctgctgtgcg gtgactccca aaatcttgat aacaacaagg	420
taaccgaatc gcgctaagga accccggcat ctccgggtact ctgcatatgc gtaccctta	480
agccgaattc cagcacactg gcggccgtta ctaattggat ccgaactccg taaccaagcc	540
tgatgcgtaa cttgagttat tctatagtgt ccctaaaata acctggcggt a	591

<210> 49

<211> 454

<212> DNA

<213> Homo sapien

<400> 49

aagagggtac ctgccttgaa atttaaatgt ctaaggaaar tgggagatga ttaagagttg	60
gtgtggcyta gtcacaccaa aatgtattta ttacatctg ctcttttcta gttgacagga	120
aagaaagctg ctgtggggaa aggagggata aatactgaag ggatttacta aacaaatgtc	180
catcacagag ttttctttt ttttttttg agacagagtc ttgctctgtc acccaggctg	240
gaatgaagwg gtatgatctc agttgaatgc aacctctacc tcctaggttc aagcgattct	300
catgcctcag cctcctgagc agctgggact ataggcgcat gctaccatgc caggctaatt	360
tttatatttt tattagagac ggggtgttgc catgttggcc aggcaggtct cgaactcctg	420
ggcctcagat gatctgcccc accgtacctt cttta	454

<210> 50

<211> 463

<212> DNA

<213> Homo sapien

<400> 50

aagaggggtac caaaaaaaag aaaaaggaaa aaaagaaaaa caacttgat aaggctttct 60
gctgcataca gctttttttt tttaaataaa tgggtgccaac aaatgttttt gcattcacac 120
caattgctgg ttttgaaatc gtactcttca aagggtatttg tgcagatcaa tccaatagt 180
atgccccgta ggttttgtgg actgccacg ttgtctacct tctcatgtag gagccattga 240
gagactgttt ggacatgcct gtgttcattg agccgtgatg tccggggggc gtgtacatca 300
tgttaccgtg ggggtggggc tgcattggct gctgggcata tggctgggtg cccatcatgc 360
ccatctgcat ctgcataggg tattggggcg ttgatccat atagccatga ttgctgtggt 420
agccactgtt catcattggc tgggacatgc tgttaccctc tta 463

<210> 51

<211> 399

<212> DNA

<213> Homo sapien

<400> 51

cttcaacctc ccaagtgtc gggattacag gactgagcca ccacgtcag cctaagcctc 60
tttttacta cctctaagc gatctaccac agtgatgagg ggctaaagag cagtgcatt 120
tgattacaat aatggaactt agatttatta attaacaatt tttccttagc atgttggttc 180
cataattatt aagagtatgg acttacttag aaatgagctt tcattttaag aatttcatct 240
ttgaccttct ctattagtct gagcagtatg acactatacg tattttattt aactaaccta 300
ccttgagcta ttacttttta aaaggctata tacatgaatg tgtattgtca actgtaaagc 360
cccacagtat ttaattatat catgatgtct ttgagggtg 399

<210> 52

<211> 392

<212> DNA

<213> Homo sapien

<400> 52

cttcaacctc aatcaacctt ggttaattgat aaatcatca ctttaacttc tgatataatg 60
gcaataatta tctgagaaaa aaaagtgggtg aaagattaaa cttgcatttc tctcagaatc 120
ttgaaggata tttgaataat tcaaaagcgg aatcagtagt atcagccgaa gaaactcact 180
tagctagaac gttggacca tggatctaag tccctgccct tccactaac agctgattgg 240
ttttgtgtaa acctcctaca cgcttgggct tggctgcctc atttgtcaaa gtaaaggctg 300
aaataggaag ataatgaacc gtgtcttttt ggtctctttt ccatccatta ctctgatttt 360
acaaagaggc ctgtattccc ctggtgaggt tg 392

<210> 53

<211> 179

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1)...(179)

<223> n = A,T,C or G

<400> 53

ttcgggtgat gcctcctcag gctacagtga agactggatt acagaaaggt gccagcgaga 60
tttcagattc ctgtaaacct ctaaagaaaa ggagtcgcgc ctcaactgat gtagaaatga 120
ctagttcagc atacngagac acntctgact ccgattctag aggactgagt gacctgcan 179

<210> 54

<211> 112

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (112)

<223> n = A,T,C or G

<400> 54

ttcgggtgat gcctctcag gctacatcat natagaagca aagtagaana atcnngtttg 60
 tgcattttcc cacanacaaa attcaaatga ntggaagaaa ttggganagt-at 112

<210> 55

<211> 225

<212> DNA

<213> Homo sapien

<400> 55

tgagcttccg cttctgacaa ctcaatagat aatcaaagga caactttaac agggattcac 60
 aaaggagtat atccaaatgc caataaacat ataaaaagga attcagcttc atcatcatca 120
 gaagwatgca aattaaaacc ataatgagaa accactatgt cccactagaa tagataaaat 180
 cttaaaaagac tggtaaaaacc aagtgttggg aaggcaagag gagca 225

<210> 56

<211> 175

<212> DNA

<213> Homo sapien

<400> 56

gctcctcttg ccttaccac acattctcaa aaacctgtta gagtctaag cattctcctg 60
 ttagtattgg gattttaccc ctgtcctata aagatgttat gtaccaaaaa tgaagtggag 120
 ggccataccc tgagggaggg gagggatctc tagtgttgtc agaagcggaa gctca 175

<210> 57

<211> 223

<212> DNA

<213> Homo sapien

<400> 57

agccatttac caccatgga tgaatggatt ttgtaattct agctgttgta ttttgtgaat 60
 ttgttaattt tgttgttttt ctgtgaaaca catacattgg atatgggagg taaaggagtg 120
 tccagttgc tcctgggtcac tccctttata gccattactg tcttgtttct tgtaactcag 180
 gtttaggtttt ggtctctctt gctccactgc aaaaaaaaaa aaa 223

<210> 58

<211> 211

<212> DNA

<213> Homo sapien

<400> 58

gttcgaagggt gaacgtgtag gtacgggac tcacaactgg ggaactgtca aagacgaatt 60
 aactgacttg gatcaatcaa atgtgactga ggaaacacct gaaggtgaag aacatcatcc 120
 agtggcagac actgaaaata aggagaatga agttgaagag gtaaaagagg agggtcctaaa 180
 agagatgact ttggatgggt ggtaaatggc t 211

<210> 59
<211> 208
<212> DNA
<213> Homo sapien

<400> 59
gctcctcttg ccttaccaac tttgcacca tcatcaacca tytggccagg tttgcagccc 60
aggctgcaca tcaggggact gcctcgcaat acttcattgt gttgctgtg actgatgtg
120ctgtgacgga tgtggaagcc acacgtgagg ctgtggtgag tgctcgaac ctgcccattg
180
cagtgatcat tatgggtggc aaatggct 208

<210> 60
<211> 171
<212> DNA
<213> Homo sapien

<400> 60
agccatttac caccataact aaattctagt tcaaaactca acttcttcca taaacatct 60
aaccactgac accagttggc aatagcttct tctctcttta acctcttaga gtatttatgg 120
tcaatgccac acatttctgc aactgaataa agtttggtta gcaagaggag c 171

<210> 61
<211> 134
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) 2 (134)
<223> n=A,T,C or G

<400> 61
cgggtgatgc ctctcaggc tttggtgtgt cactcnact cactggctc ttctcagca 60
actggtgaan atgtctcan gaaaancnc acacgngct cagggtgggg tgggaancat 120
canaatcatc nggc 134

<210> 62
<211> 145
<212> DNA
<213> Homo sapien
<400> 62

agagggtaca tatgaacag tatataaagg aagaagtga ctgagaggaa ctcatcaag 60
gccatttaac caataagtga tagagtcaag gctcaacca ggtgtgacgg attccaggtc 120
ccaagctct tactggtacc ctctt 145

<210> 63
<211> 297
<212> DNA
<213> Homo sapien
<400> 63
tgactgaga ggaattcaaa gggtttatgc caaagaacaa accagtcctc tgcagcctaa 60
ctcatttgtt tttgggtgc gaagcatgt agagggcgt caggcagtag atggtcctc 120

ccacagtcag cgccatggtg gtccggtaaa gcatttggtc aggcaggcct cgtttcaggt 180
agacggggcac acatcagctt tctgggaaaa cttttgtagc tctggagctt tgtttttccc 240
agcataatca tacactgtgg aatcggaggt cagtttagtt ggtaaggcaa gaggagc 297

<210> 64

<211> 300

<212> DNA

<213> Homo sapien

<400> 64

gcactgagag gaacttccaa tactatgttg aataggagtg gtgagagagg gcattccttgt 60
cttgtgccgg ttttcaaagg gaatgcttcc agcttttgcc cattcagtat aatattaaag 120
aatgttttac cattttctgt cttgcctgtt tttctgagtt ttgttggtc tcttcattct 180
ccatttttag gcctttacat gtttaggaata tatttctttt aatgatactt cacttttgg 240
atcttttgtg agactctact catagtgtga taagcactgg gttggtaagg caagaggagc 300

<210> 65

<211> 203

<212> DNA

<213> Homo sapien

<400> 65

gtcctcttgg ccttaccac tcaccagta tgcagcaat tttatcrgct ttacctacga 60
aacagcctgt atccaaacac ttaacacact cacctgaaaa gttcaggcaa caatcgctt 120
ctcatgggtc tctctgctcc agttctgaac ctttctcttt tctagaaca tgcattarg 180
tcgatagaag ttctctcag tgc 203

<210> 66

<211> 344

<212> DNA

<213> Homo sapien

<400> 66

tacggggacc cctgcattga gaaagcgaga ctactctga agctgaaatg ctgttgccct 60
tgcagtgtg gtagcaggag ttctgtgctt tgtgggctaa ggctcctgga tgcacctga 120
catggagaag gcagagttgt gtgcccttc tcatggcctc gtcaaggcat catggactgc 180
cacacacaaa atgccgtttt tattaacgac atgaaattga aggagagaac acaattcact 240
gatgtggctc gtaaccatgg atatggtcac atacagaggt gtgattatgt aaagggttaat 300
tccaccacc tcatgtggaa actagcctca atgcaggggt ccca 344

<210> 67

<211> 157

<212> DNA

<213> Homo sapien

<400> 67

gcactgagag gaacttcgta gggaggttga actggctgct gaggaggggg aacaacaggg 60
taaccagact gatagccatt ggatggataa tatggtggtt gaggagggag actacttata 120
gcagaggggt gtgtatagcc tgaggaggca tcaccg 157

<210> 68

<211> 137

<212> DNA

<213> Homo sapien

<400> 68
gcactgagag gaacttctag aaagtgaag tctagacata aaataaaata aaaatttaaa 60
actcaggaga gacagcccag cacggtggct cagcctgta atcccagaac ttggggagcc 120
tgaggaggca tcacccg 137

<210> 69

<211> 137

<212> DNA

<213> Homo sapien

<400> 69
cgggtgatgc ctctcaggc tttattttga agactatcga ttggacttct tatcaactga 60
agaatccgtt aaaaatacca gttgtattat ttctacctgt caaaatccat ttcaaagtgt 120
gaagttctct tcagtcgc 137

<210> 70

<211> 220

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (220) ...

<223> n = A, T, C or G

<400> 70

agcatgttga gccagacac gcaatctgaa tgagtgtgca cctcaagtaa atgtctacac 60
gctgcctggt ctgacatggc acaccatcnc gtggagggca casctctgct cngcctacwa 120
cgagggcant ctcatwgaca ggttccaccc accaaactgc aagaggctca nnaagtactr 180
ccagggtmya sggacmasgg tgggaytyca ycacwcacat 220

<210> 71

<211> 353

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (353) ...

<223> n = A, T, C or G

<400> 71

cgttagggtc tctatccact gctaaaccat acacctgggt aaacagggac catttaacat 60
tcccanctaa atatgccaa tgacttcaca tgtttatctt aaagatgtcc aaaacgcaac 120
tgattttctc cctaaacct gtgatgggtg gatgattaan cctgagtggc ctacagcaag 180
ttaagtgcaa ggtgctaaat gaangtgacc tgagatacag catctacaag gcagtacctc 240
tcaacncagg gcaactttgc ttctcanagg gcatttagca gtgtctgaag taatttctgt 300
attacaactc acggggccgg ggggtgaatat ctantggana gnagacccta acg 353

<210> 72

<211> 343

<212> DNA

<213> Homo sapien

<400> 72

gcactgagag gaacttccaa tacyatkac agagtgaaca rgcarccyac agaacaggag 60
 aaaatgttyg caatctctcc atctgacaaa aggctaatat ccagawtcta awaggaactt 120
 aaacaaattt atgagaaaag aacaracaac ctcaawcaaaa agtgggtgaa ggawatgcta 180
 aaargaagac atytattcag ccagtaaaca yatgaaaaaa aggtcatsa tcaactgawca 240
 tttagagaaat gcaaatcaaa accacaatga gataccatct yayrccagtt agaayggtga 300
 tcattaaaar stcaggaaac aacagatgct ggacaagggtg tca 343

<210> 73
 <211> 321
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

<222> (1) (321)

<223> n = A,T,C,G

<400> 73
 gcactgagag gaacttcaga gagagagaga gaggccacc ctgtacttgg ggagagaaac 160
 agaagggtgag aaagtctttg gttctgaagc agcttctaag atcttttcatt ttgttcatt 120
 tcaaagttcc catgctgcc aagtgccatc ctttggggta ctgtttctg agctccagtg 180
 ataactcatt tatacaaggg agataccag aaaaaaagtg agcaaatctt aaaaagggtg 240
 cttgagttca gccttaata ccatcttgaa atgacacaga gaaagaanga tgttgggtgg 300
 gagggtatag agaccctaac g 321

<210> 74
 <211> 321
 <212> DNA
 <213> Homo sapien

<400> 74

gcactgagag gaacttcaga gagagagaga gaggccacc ctgtacttgg ggagagaaac 160
 agaagggtgag aaagtctttg gttctgaagc agcttctaag atcttttcatt ttgttcatt 120
 tcaaagttcc catgctgcc aagtgccatc ctttggggta ctgtttctg agctccagtg 180
 ataactcatt tatacaaggg agataccag aaaaaaagtg agcaaatctt aaaaagggtg 240
 cttgagttca gccttaata ccatcttgaa atgacacaga gaaagaanga tgttgggtgg 300
 gagggtatag agaccctaac g 321

<210> 75
 <211> 317
 <212> DNA
 <213> Homo sapien

<400> 75

gcactgagag gaacttcac atgcactgag aaatgcatgt tcacaaggac tgaagtctgg 60
 aactcagttt ctcaagttcca atcctgattc aggtgtttac cagctacaca accttaagca 120
 agtcagataa ccttagcttc ctcatatgca aaatgagaat gaaaagtact catcgtgaa 180
 ttgttttgag gattagaaaa acatctggga tgcagtagaa attcaattag tattcatttt 240
 cattcttcta aattaaacaa ataggatttt tagtgggtgga acttcagaca ccagaaatgg 300
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<210> 142

<211> 419

<212> DNA

<213> Homo sapien

<400> 142

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<210> 143

<211> 402

<212> DNA

<213> Homo sapien

<400> 143

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<210> 144

<211> 224

<212> DNA

<213> Homo sapien

<400> 144

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tgagggtgat tcacgagttg cggacaactc ctttgatgcc aagcgaggtg cagccggaga 180
ctggggagag cgagccaatc aggttttgaa gttectctca gtgc 224
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<210> 145

<211> 111

<212> DNA

<213> Homo sapien

<400> 145

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atagactttg aacaaaaagg aacatttgct ggcctgagga ggcacaccc g 111
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<210> 146

<211> 585

<212> DNA

<213> Homo sapien

<400> 146

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<210> 147

<211> 579

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (579)

<223> n = A,T,C or G

<400> 147

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<210> 148

<211> 249

<212> DNA

<213> Homo sapien

<400> 148

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aaataaatct	ttgtggtttc	agatatttag	ctatagcaga	tcaggctgac	taagagaaac	180
cccataagag	ttacatactc	attaatctcc	gtctctatcc	ccaggctctca	gatgctggac	240
aagggtgtca						249

<210> 149

<211> 255

<212> DNA

<213> Homo sapien

<400> 149

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ctttttttta	atatgcttgt	tgaccacatg	tatatcatct	tttgagaagt	gtctgttcac	180
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<210> 150

<211> 318

<212> DNA

<213> Homo sapien

<400> 150

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aacaggacac	tgtctccgct	gccacaaagc	gtcagagact	cccatctttg	aagcacggcc	240
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<210> 151

<211> 323

<212> DNA

<213> Homo sapien

<220> misc_feature

<221> (1) ... (323)

<222> n = A,T,C or G

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 gtengnaata ggggcncata actacagaaa tgcanttcac actgcttcca ntgcctatng 240
 cgtgtggcct tncctactct tcttntatc caagtagcat ctctggantg cttccccact 300
 ctccacattg ttgcagcnat aat 323

<210> 152

<211> 311

<212> DNA

<213> Homo sapien

<400> 152

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 cagagggtca g 311

<210> 153

<211> 332

<212> DNA

<213> Homo sapien

<400> 153

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<210> 154

<211> 345

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (345)

<223> n = A,T,C or G

<400> 154

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aacttgggta aggaacagga atgtggtcan cctatggaat cttga 345

<210> 155

<211> 295

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (295)

<223> n = A,T,C or G

<400> 155

gacgcttggc cacttgacac attaaacagt tttgcataat cactancatg tatttctagt 60
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aatatccttt anggccaata tatttnatgt cccttaatta agagctactg tccgt 295

<210> 156

<211> 406

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (406)

<223> n = A,T,C or G

<400> 156

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<210> 157

<211> 208

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (208)

<223> n = A,T,C or G

<400> 157

tgacgcttgg ccacttgaca cactaaaggg tgttactcat cactttcttc tctcctcggt 60
ggcatgtgag tgcatttatt cacttggcac tcatttgttt ggcagtgact gtaanccana 120
tctgatgcat acaccagctt gtaaattgaa taaatgtctc taatactatg tgctcacaat 180
anggtanggg tgaggagaag gggagaga 208

<210> 158

<211> 547

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (547)

<223> n = A,T,C or G

<400> 158

```

cttcaacctc cttcaacctc cttcaacctc ctggattcaa acaatcatcc cacctcagac      60
tccttagtag ctgagactac agactcacgc cactacatct ggctaaattt ttgtagagat      120
agggtttcat catgttgccc tggctggtct caaactcctg acctcaagca atgtgccac      180
ctcagcctcc caaagtgtgt ggattacagg cataagccac catgccagc ccatntttaa      240
tctttectac cacattctta ccacactttc ttttatgttt agatacataa atgcttacca      300
ttatgataca attgccaca gtattaagac agtaacatgc tgcacaggtt tgtagcctag      360
gaacagtagg caataccaca tagcttaggt gtgtggtaga ctataccatc taggtttgtg      420
taagttacac tttatgtctgt ttacacaatg acaaaacat ctaatgatgc atttctcaga      480
atgtatcctt gtcagtaagc tatgatgtac agggaaacact gcccaaggac acagatatgt      540
tacctgt                                           547

```

<210> 159

<211> 203

<212> DNA

<213> Homo sapien

<400> 159

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gctcctcttg ccttaccac tcaaccagta tgtcagcaat tttatcrgct ttacctacga      60
aacagcctgt atccaaacac ttaacacact cacctgaaaa gttcaggcaa caatcgcctt      120
ctcatgggtc tctctgtccc agttctgaac ctttctcttt tctagaaca tgcatttarg      180
tcgatagaag ttcctctcag tgc                                           203

```

<210> 160

<211> 402

<212> DNA

<213> Homo sapien

<400> 160

```

tgtaagtcca gcagtgtgat ggggtggaaca gggttgtaag cagtaattgc aaactgtatt      60
taaacaataa taataatatt tagcatttat agagcacttt atatcttcaa agtacttgca      120
aacattayct aattaaatc cctctctgat tataatctgg atacaaatgc acttaaacctc      180
aggacagggc catgagaraa gtagtcattt gaaagtttgt gctagctatg ctttaaaaac      240
ctatacaatg atgggraagt tagagttcag attctgttgg actgtttttg tgcatttcag      300
ttcagcctga tggcagaatt agatcatatc tgcactcgat gactytgctt gataacttat      360
cactgaaatc tgagtgttga tcatcacact gctcgactta ca                                           402

```

<210> 161

<211> 193

<212> DNA

<213> Homo sapien

<400> 161

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agcatgttga gccagacac tgaccaggag aaaaaccaac caatagaaac acgccagac      60

```


actgaccagg agaaaaacca accaataaaa acaggccccg acataagaca aataataaaa 120
ttagcggaca aggacatgaa aacagctatt gtaagagcgg atatagtgtg gtgtgtctcg 180
gctcaacatg cta 193

<210> 162

<211> 147

<212> DNA

<213> Homo sapien

<400> 162

tgttgagccc agacactgac caggagaaaa accaaccaat aaaaacaggc cgggacataa 60
gacaaataat aaaattagcg gacaaggaca tgaaaacagc tattgtaaga gcggtatag 120
tggtgtgtgt ctgggctcaa catgcta 147

<210> 163

<211> 294

<212> DNA

<213> Homo sapien

<400> 163

tagcatgttg agcccagaca caaatctttc ctttaagcaat aaatcatttc tgcataatgtt 60
tttaaaacca cagctaagcc atgattattc aaaaggacta ttgtattggg tattttgatt 120
tgggttctta tctccctcac attatcttca tttctatcat tgacctctta tcccagagac 180
tctcaaactt ttatgttata caaatcacat tctgtctcaa aaaatatctc acccacttct 240
cttctgtttc tgcgtgtgta tgtgtgtgtg tgtgtgtctg ggctcaacat gcta 294

<210> 164

<211> 412

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (412)

<223> n = A,T,C or G

<400> 164

cgggattggc tttgagctgc agatgctgcc tgtgaccgca cccggcgtgg aacagaaagc 60
cacctggctg caagtgcgcc agagccgccc tgactacgtg ctgctgtggg gctggggcgt 120
gatgaactcc accgcctga aggaagccca ggccaccgga taccgccgag acaagatgta 180
cggcgtgtgg tgggcccgtg cggagccgga tgtgcgtgac gtgggccaag gcgccaaggg 240
ctacaacgag ctggctctga acggctacgg cagcagctcc aaggatgatcc angacatcct 300
gaaacacgtg cagcacaagg gccagggcac ggggcccaca gacgaagtgg gctcgggtgt 360
gtacaccgag ggcgtgatca tccagatgct ggacaagggt tcaatcacta at 412

<210> 165

<211> 361

<212> DNA

<213> Homo sapien

<400> 165

ttgacacctt gtccagcatc tgcattctgat gagagcctca gatggctaacc actaatggca 60
gaaggcaaag gagaacaggc attgtatggc aagaaaggaa gaaagagaga ggggagaaag 120
gtgctaggtt cttttcaaca accagttctt gatggaactg agagtaagag ctcaaggcca 180
ggtgtgtgta ctccaaaccg taatcccaac attttaggag gctgaggcag gcagatgtct 240

tgaccccatg agtttgtgac cagcctgaac aacatcatga gactccatct ctacaataat 300
tacaaaaatt aatcaggcat tgtggtatgc cctgtagtcc cagatgctgg acaagggtgc 360
a 361

<210> 166

<211> 427

<212> DNA

<213> Homo sapien

<400> 166

twgactgact catgtccctt acaccctaact atctttctcca ggtggccagg catgatagaa 60
tctgatectg acttagggga atattttctt tttacttccc atcttgatgc cctgccgggtg 120
agtttctctg ttcagggtta gaaaggagct caggccaaag taatgaacaa atccatcctc 180
acagacgtac agaataagag aacwtggacw tagccagcag aacmcaaktg aaamcagaac 240
mcttamctag gatracaaac mrrraratar ktgcycmcmc wtataataga aaccaaactt 300
gtatctaatt aaatatttat ccacygtcag ggcattagtg gttttgataa atacgctttg 360
gctaggatgc ctgagggttag aatggaaraa caattgcacm gagggtaggg gacatgagtc 420
aktctaa 427

<210> 167

<211> 500

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (500)

<223> n = A,T,C or G

<400> 167

aacgtcgcat gctcccgcc gccatggccg cgggatagac tgactcatgt cccctaagat 60
agaggagaca cctgctaggt gtaaggagaa gatgggttagg tctacggagg ctccagggtg 120
ggagtagttc cctgctaagg gagggtagac tgttcaacct gttctgctc cggcctccac 180
tatagcagat gcgagcagga gtaggagaga gggaggtaag agtcagaagc ttatgtttgtt 240
tatgcgggga aacgcrtat cgggggcagc cragttatta ggggacantr tagvyartcw 300
agntagcatc caaagcngg gagttntccc atatggttgg acctgcaggc ggccgcatta 360
gtgattagca tgtgagcccc agacacgcag agcaacaagg acctaaacte agatcctgtg 420
ctgattactt aacatgaatt attgtattta tttacaact ttgagttatg aggcattatta 480
ttaggtccat attacctgga 500

<210> 168

<211> 358

<212> DNA

<213> Homo sapien

<400> 168

ttcatcgctc ggtgactcaa gcctgtaatc ccagaacttt gggaggccga ggggagcaga 60
tcacctgagg ttgggagttt gagaccagcc tggccaacat ggtgacaacc cgtctctgct 120
aaaaatacaa aaattagcca agcatggttg catgcacttg taatcccagc tactcgggag 180
gctgaggcag gagaatcact tgaggccagg aggagaggtg tgcagtgagg cagaggttga 240
gatcatgcca ctgcactcca gcctgggcaa cagagtaaga ctccatctca aaaaaaaaaa 300
aaaaaaaaaa tgatcagagc cacaaatata gaaaaccttg agtcaccgag cgatgaaa 358

<210> 169

<211> 1265

<212> DNA

<213> Homo sapien

<400> 169

ttctgtccac accaatctta gagctctgaa agaatttgtc tttaaatatac ttttaatatgt	60
aacatgtatt ttatggacca aattgacatt ttcgactatt ttttcccaa aaaagtcagg	120
tgaatttcag cactactgagt tgggaatttc ttatcccaga agwcggcacg agcaatttca	180
tatttattta agattgattc cactactccgt tttcaaggag aatccctgca gtctccttaa	240
aggtagaaca aatactttct attttttttt caccattgtg ggattggact ttaagagggtg	300
actctaaaaa aacagagaac aaatatgtct cagttgtatt aagcacggac ccatattatc	360
atattcactt aaaaaaatga tttcctgtgc acettttggc aacttctctt ttcaatgtag	420
ggaaaaactt agtcaccctg aaaaccaca aaataaataa aacttgtaga tgtgggcaga	480
argtttgagg gtggacattg tatgtgttta aattaaaccc tgtatcactg agaagctgtt	540
gtatgggtca gagaaaatga atgcttagaa gctgttcaca tcttcaagag cagaagcaaa	600
ccacatgtct cagctatatt attatttatt ttttatgcat aaagtgaatc atttcttctg	660
tattaatttc caaagggttt taccctctat ttaaagtctt tgaaaaacag tgcattgaca	720
atgggttgat atttttcttt aaaagaaaaa tataattatg aaagccaaga taatctgaag	780
cctgttttat tttaaaactt tttatgttct gtgggtgatg ttgtttgttt gtttgtttct	840
attttgttgg ttttttactt tgtttttgtt tttgtttgtt tttggtttdg cactactacat	900
gcagtttctt taaccaatgt ctgtttggct aatgtaatta aagttgttaa tttatatgag	960
tgcatttcaa ctatgtcaat ggtttcttaa tttttattgt gtagaagtac tggtaatttt	1020
tttatttaca atatgtttaa agagataaca gtttgatatg ttttcatgtg tttatagcag	1080
aagttattta tttctatggc attccagcgg atattttggt gtttgcgagg catgcagtca	1140
atattttgta cagttagtgg acagtattca gcaacgcctg atagcttctt tggccttatg	1200
ttaaataaaa agacctgttt gggatgtaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa	1260
aaaaa	1265

<210> 170

<211> 383

<212> DNA

<213> Homo sapien

<400> 170

tgtaatgcca gcagtgatgac gacgatattc ttcttattaa tgtggtaatt gaacaaatga	60
tctgtgatac tgatcctgag ctaggaggcg ctgttcagtt aatgggactt cttcgacttc	120
taattgatcc agagaacatg ctggctacaa ctaataaaac cgaaaaaagt gaatttctaa	180
attttttcta caaccattgt atgcatgttc tcacagcacc acttttgacc aatacttcag	240
aagacaaatg tgaaaaggat aatatagttg gatcaaaca aaacaacaca atttgtcccg	300
ataattatca aacagcacag ctacttgctt taattttaga gttactcaca ttttgtgtgg	360
aacatcacac tgctcgactt aca	383

<210> 171

<211> 383

<212> DNA

<213> Homo sapien

<400> 171

tgggcacctt caatatcgca agttaaaaat aatgttgagt ttattatact tttgacctgt	60
ttagctcaac aggggtgaagg catgtaaga atgtggactt ctgaggaatt ttcttttaa	120
aagaacataa tgaagtaaca ttttaattac tcaaggacta cttttggttg aagtttataa	180
tctagatacc tctacttttt gtttttgctg ttcgacagtt cacaagacc ttcagcaatt	240
tacagggtaa aatcgttgaa gtagtggagg tgaaactgaa attttaaatt attctgtaaa	300
tactataggg aaagaggctg agcttagaat ctttttggtt ttcattgtgt ctgtgctctt	360
atcatcacac tgctcgactt aca	383

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<210> 172
<211> 699
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(699)
<223> n = A,T,C or G
<400> 172
tcgggtgatg cctcctcagg cttgtcgta gtgtacacag agctgctcat gaagcgacag 60
cggctgcccc tggcacttca gaacctcttc ctctacactt ttggtgcgct tctgaatcta 120
ggctctgcatg ctggcgggcg ctctggccca ggctcctgg aaagtctctc aggatgggca 180
gcactcgtgg tgctgagcca ggcactaaat ggactgctca tgtctgctgt catggagcat 240
ggcagcagca tcacacgcct ctttgtgggt tctgtctcgc tgggtggtaa cgccgtgctc 300
tcagcagtc tgctacggct gcagctcaca gccgccttct tctggccac attgctcatt 360
ggcctggcca tgcgcctgta ctatggcagc cgctagtccc tgacaacttc caccctgatt 420
ccggaccctg tagattgggc gccaccacca gatccccctc ccaggccttc ctccctctcc 480
catcagcggc cctgtaacaa gtgccttggt agaaaagctg gagaagtgag ggcagccagg 540
ttattctctg gaggttggtg gatgaagggg tacccttagg agatgtgaag tgtgggtttg 600
gttaaggaaa tgcttaccat cccccaccc caaccaagtt nttccagact aaagaattaa 660
ggtaacatca atacctaggc ctgaggaggc atcaccgca 699

<210> 173
<211> 701
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(700)
<223> n = A,T,C or G
<400> 173
tcgggtgatg cctcctcagg ccagatcaaa cttgggggtg aaaactgtgc aaagaaatca 60
atgtcggaga aagaattttg caaaagaaaa atgcctaata agtactaatt taatagggtca 120
cattagcagt ggaagaagaa atgttgatat tttatgtcag ctattttata atcaccagag 180
tgcttagctt catgtaagcc atctcgtatt cattagaaat aagaacaatt ttattcgtcg 240
gaaagaactt ttcaatttat agcatcttaa ttgtcagga ttttaaattt tgataaagaa 300
agctccactt ttggcaggag tagggggcag ggagagagga ggctccatcc acaaggacag 360
agacaccagg gccagtaggg tagctggtgg ctggatcagt cacaacggac tgacttatgc 420
catgagaaga aacaacctcc aaatctcagt tgcttaatac aacacaagct catttcttgc 480
tcacgttaca tgctctatgt agatcaacag caggtgactc agggaccag gctccatctc 540
catatgagct tccatagtca ccaggacacg ggctctgaaa gtgtcctcca tgcaggggaca 600
catgcctctt cctttcattg ggcagagcaa gtcacttatg gccagaagtc acactgcagg 660
gcagtgccat cctgctgtat gcctgaggag gcacccccga 701

<210> 174
<211> 700
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(700)
<223> n = A,T,C or G
<400> 174
tcgggtgatg cctcctcagg ccctaaatc agagtccagg gtcagagcca caggagacag 60

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ggaaagacat agattttaac cggccccctt caggagattc tgaggctcag ttcactttgt 120
tgcagtttga acagaggcag caaggctagt ggtaggggc acggtctcta aagctgcact 180
gcctggatct gcctcccagc tctgccagga accagctgcg tggccttgag ctgetgacac 240
gcagaaagcc cctgtggac ccagctctct cgtctgtaag atgaggacag gactctagga 300
accctttccc ttggtttggc ctcactttca caggctccca tcttgaactc tatctactct 360
tttctgaaa ccttgtaaaa gaaaaaagtg ctagecctggg caacatggca aaacctgtc 420
tctacaaaa atacaaaaat tagttgggtg tggtaggcag tgctgtagt cccagccact 480
tgggaggtgc tgaggtggga ggatcacttg agcccgagg gtggaggttg cagtgcagca 540
agatcatgcc actgcactcc agcctgagta atagagtaag actctgtctc aaaaacaaca 600
acaacaacg tgagtgtgcc tctgtttccg ggttgatgg ggcaccacat ttatgcactc 660
ctcagatttg gacgtgcag cctgaggagg catcacccga 700

```

<210> 175

<211> 484

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) (484)

<223> n = A,T,C or G

<400> 175

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tatagggcga attgggcccg agttgcatgn tcccggccgc catggccgcg ggattcgggt 60
gatgcctcct caggcttgte tgccacaagc tacttctctg agctcagaaa gtgccccttg 120
atgagggaaa atgtcctact gactgcgaa tttctcagtt ccattttacc tccagctcct 180
ccttctaaac cagttaataa attcattcca caagtattta ctgattacct gcttgtgcca 240
gggactatto tcaggctgaa gaaggtggga ggggagggcg gaacctgagy agccacctga 300
gccagcttta tatttcaacc atggctggcc catctgagag catctcccca ctctgcgcaa 360
cctatcgggg catagcccag ggatgcccc aggcggccca ggtagatgc gtccttttgg 420
cttgtcagtg atgacataca ccttagctgc tttagctggtg ctggcctgag gaggcatcac 480
ccga

```

<210> 176

<211> 432

<212> DNA

<213> Homo sapien

<400> 176

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tcgggtgatg cctctcagg gctcaaggga tgagaagtga cttctttctg gagggaccgt 60
tcatgccacc caggatgaaa atggataggg acccacttgg aggacttgc gatatgtttg 120
gacaaatgcc aggtagcgga attggtactg gtccaggagt tatccaggat agattttcac 180
ccaccatggg acgtcatcgt tcaaatcaac tcttcaatgg ccatggggga cacatcatgc 240
ctcccacaca atcgcagttt ggagagatgg gaggcaagtt tatgaaaagc caggggctaa 300
gccagctcta ccataaccag agtcaggga tcttatccca gctgcaagga cagtcgaagg 360
atatgccacc tcggttttct aagaaaggac agcttaatgc agatgagatt agcctgagga 420
ggcatcccc ga 432

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<210> 177

<211> 788

<212> DNA

<213> Homo sapien

<400> 177

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tggcaatgcc	agtggaacca	cgctgcttga	ggctctggac	tgcacccac	caccaactcg	180
cccaactgac	aagcccttgc	gcctgcctct	ccaggatgtc	tacaaaattg	gtggtattgg	240
tactgttcct	gttggccgag	tggagactgg	tgttctcaaa	cccggtatgg	tggtcacctt	300
tgctccagtc	aacgtttaca	cggaagtaaa	atctgtcgaa	atgcaccatg	aagctttgag	360
tgaagctctt	cctggggaca	atgtgggctt	caatgtcaag	aatgtgtctg	tcaaggatgt	420
tcgtcgtggc	aacgtttgct	gtgacagcaa	aaatgaccca	ccaatggaag	cagctggcct	480
cactgctcag	gtgattatcc	tgaaccatcc	aggccaaata	agtgcgggct	atgcccctgt	540
attggattgc	cacacggctc	acattgcatg	caagtttgct	gagctgaagg	aaaagattga	600
tcgccgttct	ggtaaaaagc	tggagatgg	ccctaaattc	ttgaagtctg	gtgatgctgc	660
cattgttgat	atggttcctg	gcaagcccat	gtgtgttgag	agcttctcag	actatccacc	720
tttgggtcgc	tttgcgttgc	gtgatatgag	acagacagtt	gcgggtgggtg	tctgggctca	780
acatgcta						788

<210> 178

<211> 786

<212> DNA

<213> Homo sapien

<400> 178

tagcatgttg	agcccagaca	cctgtgtttc	tgggagctct	ggcagtggcg	gattcatagg	60
cacttgggct	gcactttgaa	tgacacactt	ggctttatta	gattcactag	tttttaaaaa	120
attgttggtc	gtttcttttc	attaaagggt	taatcagaca	gatcagacag	cataattttg	180
tatttaatga	cagaaacgtt	ggtagatttc	ttcatgaatg	agcttgcatt	ctgaagcaag	240
agcctacaaa	aggcacttgt	tataaatgaa	agttctgggt	ctagaggcca	gtactctgga	300
gtttcagagc	agccagtgat	tgttccagtc	agtgtgcct	agttatatag	aggaggagta	360
cactgtgcac	tcttctaggt	gtaagggtat	gcaactttgg	atcttaaaat	tctgtacaca	420
tacacacttt	atatatatgt	atgtatgtat	gaaaacatga	aattagtttg	tcaaataatg	480
gtgtgtttag	tatttttagc	tagtgcaact	atttccacat	tatttattaa	attgatctaa	540
gacactttct	tgttgacacc	ttgaatatta	atgttcaagg	gtgcaatgtg	tattccttta	600
gattgttaaa	gcttaattac	tatgatttgt	agtaaattaa	cttttaaaat	gtatttgagc	660
ccttctgtag	tgctgtaggg	ctcttacagg	gtgggaaaga	ttttaatttt	ccagttgcta	720
attgaacagt	atggcctcat	tatatatttt	gatttatagg	agtttgtgtc	tgggctcaac	780
atgcta						786

<210> 179

<211> 796

<212> DNA

<213> Homo sapien

<400> 179

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gcttttaaaa	agccagtga	cctttttaat	actttggcaa	ccttctttca	caggcaaaga	120
acaccccat	ccgcccttgc	tttggagtgc	agagtttggc	tttggttctt	tgccttgctt	180
ggagtatact	tctaattcct	gttgtcctgc	acaagctgaa	taccgagcta	cccaccgcca	240
cccaggccag	gtttccactc	atttattact	ttatgtttct	gttccattgc	tgggtccacag	300
aaataagttt	tcctttggag	gaatgtgatt	ataccctttt	aatttctctc	ttttgctttt	360
ttttaatatc	attggtatgt	gtttggccca	gaggaaactg	aaattcacca	tcattctgac	420
tggcaatccc	attaccatgc	tttttttaaa	aaacgtaatt	tttcttgctt	tacattggca	480
gagtagccct	tcctggctac	tggcttaaatg	tagtactca	gtttctaggt	ggcattaggc	540
atgagacctg	aagcacagac	tgtcttacca	caaaaggtga	caagatctca	aaccttagcc	600
aaagggctat	gtcaggtttc	aatgctatct	gcttctgttc	ctgctcactg	ttctggattt	660
tgctcttctt	cctccctagc	accagaattt	cccagctctc	ctccctacct	tccttggttt	720
taattctaata	ctatcagcaa	aataactttt	caaagtgttt	aaccggtatc	tccatgtgtc	780
tgggctcaac	atgcta					796

<210> 180

<211> 488

<212> DNA

<213> Homo sapien

<400> 180

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ggatgtgctg caaggcgatt aagttgggta acgccagggt tttcccagtc acgacgttgt 60
aaaacgacgg ccagtgaatt gtaatacgac tcactatagg gogaattggg- cccgacgtcg 120
catgtcccgg gccgccatgg ccgcgggata gcatgttgag cccagatacc tgcagggtcat 180
ttggagagat ttttcacgtt accagcttga tggctctttt caggaggaga gacactgagc 240
actcccgaagg tgaggttgaa gatttcctct agatagccgg ataagaagac taggagggat 300
gcctagaaaa tgattagcat gcaaatttct acctgccatt tcagaactgt gtgtcagccc 360
acattcagct gcttcttgtg aactgaaaag agagagggtat tgagactttt ctgatggcgg 420
ctctaacatt gtaacacagt aatctgtgtg tgtgtgggtg tgtgtgtgtg tctgggctca 480
acatgcta 488

```

<210> 181

<211> 317

<212> DNA

<213> Homo sapien

<400> 181

```

tagcatgttg agccagaca cggcgacggg acctgatgag tggggtgatg gcacctgtga 60
aaaggaggaa cgtcatcccc catgatattg gggaccaga tgatgaacca tggctccggc 120
tcaatgcata tttaatccat gatactgctg attggaagga cctgaacctg aagtttgtgc 180
tgcaggttta tggggactat tacctcagcg gtgatcaaaa ctctctgaag gacatgtggc 240
ctgtgtgtct agtaagggat gcacatgcag tggccagtgt gccaggggta tggttgggtg 300
ctgggctcaa catgcta 317

```

<210> 182

<211> 507

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (507)

<223> n = A,T,C or G

<400> 182

```

tagcatgttg agccagaca ctggctgtta gccaaatcct ctctcagctg ctccctgtgg 60
tttggtgact caggattaca gaggcacctt gtttcaggga acaaaaagat ttttagctgcc 120
agcagagagc accacataca ttagaatggt aaggactgcc acctccttca agaacaggag 180
tgagggttgg ggtgaatggg aatggaagcc tgcattccct gatgcatttg tgctctctca 240
aatcctgtct tagtcttagg aaaggaagta aagtttcaag gacggttccg aactgctttt 300
tgtgtctygg ctcaacatgc tatccgcggg ccatggcgcc cgggagcatg cgacgtcggg 360
cccaattcgc cctatagtga gtctgtattac aattcactgg ccgtcgtttt acaacgtcgt 420
gactgggaaa accctggcgt tacccaactt aatcgcttgg cagcacatcc ccttttccca 480
gctggcgtaa tancgaaaag gcccgca 507

```

<210> 183

<211> 227

<212> DNA

<213> Homo sapien

<400> 183

gatttacgct gcaacactgt ggaggtagcc ctggagcaag gcaggcatgg atgtttctgc 60
aatcccaaaa tggagcctgg tatttcagcc aggaatctga gcagagcccc ctctaattgt 120
agcaatgata agttattctc tttgttcttc aaccttccaa tagccttgag cttccagggg 180
agtgtcggtta atcattacag cctggtctcc acagtgttgc agcgtaa 227

<210> 184

<211> 225

<212> DNA

<213> Homo sapien

<400> 184

ttacgctgca acactgtgga gcagattaac atcagacttt tctatcaaca tgactggggt 60
tactaaaaag acaacaaatc aatggcttca aaagtctaag gaataatttc gatacttcaa 120
ctttataaaa cctgacaaaa ctatcaatca agcataaaga cagatgaaga acatttccag 180
atthtggcca atcagatatt ttacctccac agtgttgcag cgtaa 225

<210> 185

<211> 597

<212> DNA

<213> Homo sapien

<400> 185

ggcccgacgt cgcattgtcc cggccgccat ggcccgggga ttctgttaggg tctctatcca 60
ctgggacca taggttagtc agagtattta gagttgagtt cctttctgct tcccagaatt 120
tgaaagaaaa ggagttaggt gatagagctg agagatcaga tttgctctg aagcctgttc 180
aagatgtatg tctcagacc ccaccactgg ggccgtgtggg tgaggctctg ggcattctatt 240
tgaatgaatt gctgaagggg agcactatgc caaggaaggg gaaccatcc tggcactggc 300
acaggggtca ccttatccag tctcagtgct ttctttgctg ctacctggtt ttctctcata 360
tgtgaggggc aggtagaag aagtgcctcg tgttgtgcga gttttagaac atctaccagt 420
aagtggggaa gtttcacaaa gcagcagctt tgttttgtgt attttcacct tcagttagaa 480
gaggaaggct gtgagatgaa tgtagttga gtggaaaaga cgggtaagct tagtggatag 540
agaccctaac gaatcactag tgcggccgcc ttgcaggtcg accatatggg agagctc 597

<210> 186

<211> 597

<212> DNA

<213> Homo sapien

<400> 186

ggcccgaaat tgcattgtcc cggccgccat ggcccgggga ttctgttaggg tctctatcca 60
ctacctaaaa aatcccaaac atataactga actcctcaca cccaattgga ccaatccatc 120
accacagagg cctacagatc ctcttttgat acataagaaa atttcccaa actacctaac 180
tatatcattt tgcaagattt gttttaccaa attttgatgg cctttctgag cttgtcagtg 240
tgaaccacta ttacgaacga tcggatatta actgccccct accgtccagg tgtagctggc 300
aacatcaagt gcagtaaata ttcattaagt tttcacctac taagggtgctt aaacacccta 360
gggtgcccag tcggttagcag atcttttgat ttgtttttat ttcccataag ggtcctgttc 420
aaggtaactc atacatgtag tgtgagcagc tagtcactat cgcattgactt ggaggggtgat 480
aatagaggcc tcttttgctg ttaaagaact cttgtcccag cctgtcaaag tggatagaga 540
ccctaacgaa tcaatagtgc ggccgcctgc aggtcgacca tatgggagag ctcccaa 597

<210> 187

<211> 324

<212> DNA

<213> Homo sapien

<400> 187

```
tcgttagggg ctctatccac ttgcaggtaa aatccaatcc tgtgtatata ttatagtctt 60
ccatatgtag tgggtcaaga gactgcagtt ccagaaagac tagccgagcc catccatgtc 120
ttccacttaa cctgctttg ggttacacat cttaactttt ctgttcaagt ttctctgtgt 180
agtttatagc atgagtattg ggawaatgcc ctgaaacctg acatgagatc tgggaaacac 240
aaacttactc aataagaatt tctcccatat ttttatgatg gaaaaatttc acatgcacag 300
aggagtggat agagacccta acga 324
```

<210> 188

<211> 178

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (178)

<223> n = A,T,C or G

<400> 188

```
gcgcggggat tcgggggtgat acctcctcat gccaaaatac aacgtntaat ttcacaactt 60
gccttccaat ttacgcattt tcaatttgc tccccattt gttgagtcac aacaaacacc 120
attgcccgaga aacatgtatt acctaactg cacatactct taaaactact catccctt 178
```

<210> 189

<211> 367

<212> DNA

<213> Homo sapien

<400> 189

```
tgacaccttg tccagcatct gacacagtct tggctcttgg aaaatattgg ataaatgaaa 60
atgaatttct ttagcaagtg gtataagctg agaatatagc tatcacatat cctcattcta 120
agacacattc agtgtccctg aaattagaat aggacttaca ataagtgtgt tcaattttctc 180
aatagctgtt attcaattga tggtaggcct taaaagtcaa agaaatgaga gggcatgtga 240
aaaaaagctc aacatcactg atcattagaa aacttccatt caaaccccca atgagatacc 300
atctcatacc agtcagaatg gctattatta aaaagtcaaa aaataacaga tgctggacaa 360
ggtgtca 367
```

<210> 190

<211> 369

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (369)

<223> n = A,T,C or G

<400> 190

```
gacaccttgt ccagcatctg acaacgctaa cagcctgagg agatctttat ttatttattt 60
agtttttact ctggctaggc agatggtggc taaaacattc atttaccat ttattcattt 120
aattgttctt gcaaggccta tggatagagt attgtccagc actgctctgg aagctaggag 180
catggggatg aacaagatag gctacatcct gttccacag aacttccact ttagtctggg 240
aaacagatga tatatacaa tatataaatg aattcaggta gttttaagta cgaaaagaat 300
```

aagaaagcag agtcatgatt tanaatgctg gaaacagggg ctattgcttg agatattgaa 360
ggtgcccaa 369

<210> 191

<211> 369

<212> DNA

<213> Homo sapien

<400> 191

tgacaccttg tccagcatct gcacagggaa aagaaactat tatcagagtg aacaggcaac 60
ctacagaatg ggagaaaatt tttgcaatct atccatctga caaagggcta atatccagaa 120
tctacaaaaga acttatacaa atttacaaga aacaaacaaa caaacaactc ctcaaaaagt 180
gggtgaagga tgtgaacaga cacttctcaa aagaagacat ttatggggcc acaaacata 240
tgaaaaaaag ctcacatca ctggctacta gataaatgca aatcaaaacc acaatgagat 300
accatctcat tccagttaga atggcaatca ttaaaaagtc aggaaacaac agatgctgga 360
caaggtgtc 369

<210> 192

<211> 449

<212> DNA

<213> Homo sapien

<400> 192

tgacgcttgg ccacttgaca cttcatcttt gcacagaaaa acttctttac agatttaatt 60
caagactggg ctagtgcag tctccagac attttttcat ttgttccata tacgtggaat 120
tttaaaatca tgtttcatca gtttgaaatg atttgggctg ctaatcaaca caattggatc 180
gactgttcta ctaaacaaca ggaaaatgtg tatctggcag cctgtggaga aacactaaac 240
attgattttt ctttgccttt tacggacttt gttccagcta catgtaatac caagttctct 300
ttaagaggag aagatgttga tcttcatttg tttctaccag actgccacc tagtaaatat 360
tctttattta tgctggtaaa aaattgccat ccaaataaga tgattcatga tactgggtatt 420
cctgctgagt gtcaagtggc caagcgtca 449

<210> 193

<211> 372

<212> DNA

<213> Homo sapien

<400> 193

tgacgcttgg ccacttgaca ccagggatgt akcagttgaa tataatcctg caattgtaca 60
tattggcaat ttcccatcaa acattctaga aagagacaac caggattgct aggccataaa 120
agctgcaata aataactggg aattgcagta atcatttcag gccattcaa tccagtttgg 180
ctcagaggtg cctttggctg agagaagagg tgagatataa tgtgttttct tgcaacttct 240
tggaagaata actccacaat agtctgagga ctagatacaa acctatttgc cattaagca 300
ccagagtctg ttaattccag tactgataag tgttgagat tagactccag tgtgtcaagt 360
ggccaagcgt ca 372

<210> 194

<211> 309

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(309)

<223> n = A,T,C or G

<400> 194

```

tgacgcttgg ccacttgaca cttatgtaga atccatcgtg ggctgatgca agccctttat 60
ttaggcttag tgttgtgggc accttcaata tcacactaga gacaaacgcc acaagatctg 120
cagaaacatt cagttctgan cactcgaatg gcaggataac tttttgtgtt gtaatccttc 180
acatatataa aaacaaactc tgcantctca cgttacaaaa aaacgtactg ctgtaaaaata 240
ttaagaaggg gtaaaggata ccatctataa caaagtaact tacaactagt gtcaagtggc 300
caagcgtca 309

```

<210> 195

<211> 312

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(312)

<223> n = A,T,C or G

<400> 195

```

tgacgcttgg ccacttgaca cccaatctcg cacttcatcc tcccagcacc tgatgaagta 60
ggactgcaac tatccccact tcccagatga ggggaccaan gtacacatta ggaccgggat 120
gggagcacag atttgcoga tcccagactc caagcactca gcgtcactcc aggacagcgg 180
ctttcagata aggtcacaaa catgaatggc tccgacaacc ggagtcagtc cgtgctgagt 240
taaggcaatg gtgacacgga tgcacgtgtn acctgtaatg gttcatcgta agtgtaagt 300
ggccaagcgt ca 312

```

<210> 196

<211> 288

<212> DNA

<213> Homo sapien

<400> 196

```

tgtatcgacg tagtggtctc ctacgccatg cagaactgtg actcaattaa acctctttcc 60
tttatgaatt acccaatctc gggtagtgtc tttatagtag tgtgagaatg gactaataca 120
agtacatttt acttagtaat aataataaac aaatatatta catttttgtg tatttactac 180
accatatttt ttattgttat tgtagtgtag accttctact tattaaaaga aataggcccg 240
aggcgggagc atcaccgaggt caggagatgg agaccactac gtcgatac 288

```

<210> 197

<211> 289

<212> DNA

<213> Homo sapien

<400> 197

```

ttgggcacct tcaatatcat gacaggtgat gtgataacca agaaggctac taagtgatta 60
atgggtgggt aatgtatata gagtaggtac actggacaga ggggtaattc atagccaagg 120
caggagaagc agaatggcaa aacatttcat cacactactc aggatagcat gcagtttaaa 180
acctataagt agtttatttt tggaattttc cacttaatat tttcagactg caggtaacta 240
aactgtggaa cacaagaaca tagataaggg gagaccacta cgtcgatac 289

```

<210> 198

<211> 288

<212> DNA

<213> Homo sapien

<400> 198

gtatcgacgt	agtgggtctcc	caagcagtg	gaagaaaacg	tgaaccaatt	aaaatgtatc	60
agatacccca	aagaaaggcg	cttgagtaaa	gattccaagt	gggtcacaat	ctcagatctt	120
aaaattcagg	ctgtcaaaga	gatttgctat	gaggttgctc	tcaatgactt	caggcacagt	180
cggcaggaga	ttgaagccct	ggccattgtc	aagatgaagg	agctttgtgc	catgtatggc	240
aagaaagacc	ccaatgagcg	ggactcctgg	agaccactac	gtcgatac		288

<210> 199

<211> 1027

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1027)

<223> n = A,T,C or G

<400> 199

gcttttttggg	aaaaacncaa	ntgggggaaa	gggggnttnn	tngcaagggg	ataaaggggg	60
aancccgagg	tttcccat	cagggaggtg	taaaaagncg	gccaggggat	tgtaanagga	120
ttcaataata	gggggaatgg	gccnngaagt	tgcaagggtc	cngcccgcca	tgnccgcggg	180
atttagtgac	attacgacgs	tggtataaaa	gtgggsccaa	waaatatitg	tgatgtgatt	240
tttsgaccag	tgaaccatt	gwacaggacc	tcatttctcty	tgagatgrta	gccataatca	300
gataaaagrt	tagaagtytt	tctgcacgtt	aacagcatca	ttaaatggag	tggtcatcacc	360
aatttcaccc	tttgtagcc	gataccttcc	ccttgaaggc	attcaattaa	gtgaccaatc	420
gtcatcacgag	aggggatggc	atggggattg	atgatgat	caggggtgat	accttcacag	480
gtgaaaggca	tatcctcttg	tctatactga	ataccacaag	tacccttttg	accatgtcga	540
ctagcaaatt	tgtctccaat	ctgtgtwac	cctaacagag	cgtaccctta	ttttacaaaa	600
tttatatcct	tctgtattga	gagttaccat	aacctgatcc	acaatgcccg	tctcgtwtgt	660
tctgagaaaa	gtgctacagt	ctctcttggt	atagcgteta	ttgggtgctct	ccaattcatc	720
ttcatttttc	aggcaagggtg	aactgttttg	cctataataa	cmtcatctcc	tgatacmcga	780
aacccckgga	rcatcaaac	catcatcatc	cagcgttckt	watgtymcta	aatccctatt	840
gcggccgcct	gcaggtcaac	atatnggaaa	acccccacc	ccttnggagc	ntaccttgaa	900
ttttccatat	gtcccntaaa	ttanctngnc	ttanctggc	cntaacctnt	tccgggtttaa	960
attgtttccg	ccccnttcc	ccncttnna	accggaaacc	ttaattttna	acngggggtt	1020
cctatcc						1027

<210> 200

<211> 207

<212> DNA

<213> Homo sapien

<400> 200

agtgacatta	cgacgtggc	catcttgaat	cctagggcat	gaagttgccc	caaagttag	60
cacttggtta	agcctgatcc	ctctggttta	tcacaaagaa	taggatggga	taaagaaagt	120
ggacacttaa	ataagctata	aattatatgg	tccttgtcta	gcaggagaca	actgcacagg	180
tatactacca	gcgtcgtaat	gtcacta				207

<210> 201

<211> 209

<212> DNA

<213> Homo sapien

<400> 201

tgggcacctt caatatctat taaaagcaca aatactgaag aacacaccaa gactatcaat 60
gaggttacat ctggagtcct cgatatatca ggaaaaaatg aagtgaacat tcacagagtt 120
ttacttcttt gggaactcaa atgctagaaa agaaaagggg gccctctttc tctggcttcc 180
tggtcctatc cagcgtcgta atgtcacta 209

<210> 202

<211> 349

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (349)

<223> n = A,T,C or G

<400> 202

ntacgttgca acactgtgga gccactgggt tttattcccg gcagggtatc cagcaaacag 60
tcaactgaaca caccgaagac cgtgggtatg taaccgttca cagtaatcgt tccagtcgtc 120
tgccgggaccc cgacgagcgt cactgggtac agaccagatt cagccggaag agaaagcgcc 180
gcaggggagag actcgaactc cactccgctg gtgagcagcc ccattgtttc aactcgaagt 240
tcaaaccggca ttgggttata taccatcagc tgaacttcac acacatctcc ttgaaccac 300
tggaatctta tttcttgggt ccgtctttct ccacagtgtt gcagcgtaa 349

<210> 203

<211> 241

<212> DNA

<213> Homo sapien

<400> 203

tgctcctctt gccttaccaa cccaaagccc actgtgaaat atgaagtga tgaacaaatt 60
cagttttcaa cgcaatatag tatagtttat ctgattcttt tgatctccag gacactttaa 120
acaactgcta ccaccaccac caacctaggg atttaggatt ctccacagac cagaaattat 180
ttctcctttg agtttcaggc tctctggga ctctgttca tcaatgggtg gtaaatggct 240
a 241

<210> 204

<211> 248

<212> DNA

<213> Homo sapien

<400> 204

tagccattta ccaccatct gcaaaccswg acmwwcargr cywgwackya ggcgatttga 60
agtactggta atgctctgat catgttagtt acataagtgt ggtcagttta caaaaattca 120
cagaactaaa tactcaatgc tatgtgttca tgtctgtgtt tatgtgtgtg taatgtttca 180
attaagtttt tttaaaaaaa agagatgatt tccaaataag aaagccgtgt tggtaaggca 240
agaggagc 248

<210> 205

<211> 505

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (505)

<223> n = A,T,C or G

<400> 205

```

tacgtctgcaa cactgtggag ccattcatac aggtccctaa ttaaggaaca agtgattatg    60
ctacctttgc acggttaggg tacgcgggcc gttaaacatg tgctactggg caggcgggtgc    120
ctctaatact ggtgatgcta gaggtgatgt ttttggtaaa caggcggggg aagatttgcc    180
gagttccttt tacttttttt aacctttcct tatgagcatg cctgtgttgg gttgacagtg    240
ggggtaataa tgacttggtg gttgattgta gatattgggc tgttaattgt cagttcagtg    300
ttttaatctg acgcaggcct atgcggagga gaatgttttc atgttactta tactaacatt    360
agttcttcta tagggtgata gattgggtcca attgggtgtg aggagttcag ttatatgttt    420
gggatttttt aggtagtggg tgttgancct gaacgcttcc ttaattgggt gctgctttta    480
rgcctactat gggtggtaaa tggct                                     505

```

<210> 206

<211> 179

<212> DNA

<213> Homo sapien

<400> 206

```

tagactgact catgtcccct accaaagccc atgtaaggag ctgagttcct aaagactgaa    60
gacagactat tctctggaga aaaataaaat ggaaattgta ctttaaaaaa aaaaaaaatc    120
ggccgggcat ggtagcacac acctgtaac ccagctacta ggggacatga gtcagtcta    179

```

<210> 207

<211> 176

<212> DNA

<213> Homo sapien

<400> 207

```

agactgactc atgtccccta cccaccttc tgctgtgctg ccgtgttccct aacagggtcac    60
agactggtag tggtcagtgg cctggggggt ggggacctct attatatggg atacaaattt    120
aggagttgga attgacacga tttagtgtact gatgggatat gggtggtaaa tggcta    176

```

<210> 208

<211> 196

<212> DNA

<213> Homo sapien

<400> 208

```

agactgactc atgtccccta tttacaggg tctctagtgc tgtgaaaaaa aaaaatgctg    60
aacattgcat ataacttata ttgtaagaaa tactgtacaa tgactttatt gcactctgggt    120
agctgtaagg catgaaggat gccagaagt ttaaggaata tgggtggtaa atggctaggg    180
gacatgagtc agtcta                                     196

```

<210> 209

<211> 345

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (345)

<223> n = A,T,C or G

<400> 209

gacgcttggc cacttgacac cttttatttt ttaaggattc ttaagtcatt tangtnactt 60
tgtaagtttt tctgtgccc ccataagaat gatagcttta aaaattatgc tggggtagca 120
aagaagatac ttctagcttt agaattgtga ggtatagcca ggattcttgt gaggaggggt 180
gatttagagc aaatttctta ttctccttgc ctcatctgta acatggggat aataatagaa 240
ctggcttgac aaggttggaa ttagtattac atggtaaaat catgtaaaat gtttagaatg 300
gtgccaagta tctaggaagt acttgggcat ggggtgtaaa tggct 345

<210> 210

<211> 178

<212> DNA

<213> Homo sapien

<400> 210

gacgcttggc cacttgacac tagagtaggg tttggccaac tttttctata aaggaccaga 60
gagtaaatat ttcaggcttt gtgggttggt cagtctctct tgcaactact cagctctgcc 120
attgtagcat agaaatcagc catagacagg acagaaatga atgggtggta aatggcta 178

<210> 211

<211> 454

<212> DNA

<213> Homo sapien

<400> 211

tgggcacctt caatatctat ccagcgcac taaattcgct tttttcttga ttaaaaattt 60
caccacttgc tgtttttgct catgtatacc aagtagcagt ggtgtgaggc catgcttggt 120
ttttgattcg atatcagcac cgtataagag cagtgccttg gccattaatt tatcttcatt 180
gtagacagca tagtgtagag tggatatctc atactcatct ggaatatttg gatcagtgcc 240
atgttccagc aacattaacg cacattcatc ttcttggcat tgtacggcct ttgtcagagc 300
tgtcctcttt ttgttttcaa gacattaag ttgacatcgt ctgtccagca cgagttttac 360
tacttctgaa ttccatttgg cagaggccag atgtagagca gtctcttttt gcttgcctt 420
cttgttcaca tcagtgtccc tgaacataac ggaa 454

<210> 212

<211> 337

<212> DNA

<213> Homo sapien

<400> 212

tccgttatgc caccagaaa acctactgga gttacttatt aacatcaagg ctggaacctt 60
tttgctcag tcttatctga ttcattgagc catggttatt actgatcga ttgaaaacat 120
tgatcacctg ggtttcttta tttatcgact gtgtcatgac aaggaaactt acaaactgca 180
acgcagagaa actattaaag gtattcagaa acgtgaagcc agcaattgtt tcgcaattcg 240
gcattttgaa aacaaatttg ccgtggaaac tttaatttgt tcttgaacag tcaagaaaaa 300
cattattgag gaaaattaat atcacagcat aacggaa 337

<210> 213

<211> 715

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(715)

<223> n = A,T,C or G

<400> 213

tcgggtgatg	cctcctcagg	catcttccat	ccatctcttc	aagattagct	gtcccaaatg	60
tttttccttc	tcttctttac	tgataaattt	ggactccttc	ttgacactga	tgacagcttt	120
agtatccttc	ttgtcacctt	gcagacttta	aacataaaaa	tactcattgg	ttttaaaagg	180
aaaaaagtat	acattagcac	tattaagctt	ggccttgaaa	cattttctat	cttttattaa	240
atgtcgggta	gctgaacaga	attcatttta	caatgcagag	tgagaaaaga	agggagctat	300
atgcatttga	gaatgcaagc	attgtcaaat	aaacatttta	aatgctttct	taaagtgagc	360
acatacagaa	atacatthaag	atattagaaa	gtgtttttgc	ttgtgtacta	ctaattaggg	420
aagcaccttg	tatagttcct	cttctaaaat	tgaagtagat	tttaaaaacc	catgtaattt	480
aattgagctc	tcagttcaga	ttttaggaga	attttaacag	ggatttggtt	ttgtctaaat	540
tttgtcaatt	tnnttagtta	atctgtataa	ttttataaat	gtcaaactgt	atttagtccg	600
ttttcatgct	gctatgaaag	aaatacccan	gacagggtta	tttataaang	gaaagangtt	660
aatttgactc	ccagttcaca	ggcctgagga	ngnatcnccc	gaaatcctta	ttgcg	715

<210> 214

<211> 345

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(345)

<223> n = A, T, C or G

<400> 214

ggtaangngc	atacntcgtg	gctcggcg	ccggagtcgg	gggattcggg	tgatgcctcc	60
tcaggcccac	ttgggcctgc	ttttcccaa	tggcagctcc	tctggacatg	ccattccttc	120
tcccacctgc	ctgattcttc	atatgttggg	tgtccctggt	tttctgggtg	tatttctctga	180
ctgctgttca	gctgccactg	tcctgcaaag	cctgcctttt	taaatgcctc	accattcctt	240
catttgtttc	ttaaatatgg	gaagtgaag	tgccacctga	ggccgggcac	agtggctcac	300
gcctgtaatc	ccagcacttt	gggagcctga	ggaggcatca	ccga		345

<210> 215

<211> 429

<212> DNA

<213> Homo sapien

<400> 215

ggtgatgcct	cctcaggcga	agctcaggga	ggacagaaac	ctcccgtgga	gcagaagggc	60
aaaagctcgc	ttgatcttga	ttttcagtac	gaatacagac	cgtgaaagcg	gggcctcacg	120
atcctttetga	cctttttgggt	tttaagcagg	aggtgtcaga	aaagttacca	cagggataac	180
tggettgtgg	cggccaagcg	ttcatagcga	cgctgccttt	tgatccttcg	atgtcggctc	240
ttcctatcat	tgtgaagcag	aattcaccaa	gcgttggtatt	gttcaccac	taatagggaa	300
cgtgagctgg	gttttagaccg	tcgtgagaca	ggtagttttt	accctactga	tgatgtgtkg	360
ttgccatggt	aatcctgctc	agtacgagag	gaaccgcagg	ttcasacatt	tggtgtatgt	420
gcttgccctt						429

<210> 216

<211> 593

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(593)

<223> n = A,T,C or G

<400> 216

tgacacctat	gtccngcatc	tggtcacagt	ttccacaaat	agccagcctt	tgccacctc	60
tctgtcctga	gggtatacaag	tatatcagga	gggtgtatacc	ttctcttctc	ttccccacca	120
aagagaacat	gcaggctctg	gaagctgtct	taggagcctt	tggtgtcaga	atttcagagt	180
cttgggtacc	ttggatgtgg	tctggaagga	gaaacattgg	ctctggataa	ggagtacagc	240
cggaggaggg	tcacagagcc	ctcagctcaa	gcccctgtgc	cttagtctaa	aagcagcttt	300
ggatgaggaa	gcaggttaag	taacatacgt	aagcgtacac	aggtagaaag	tgctgggagt	360
cagaattgca	cagtgtgtag	gagtgtacc	tcaatcaatg	agggcaaata	aactgaaaga	420
agaagaccna	ttaatgaatt	gcttanggga	aaggatcaag	gctatcatgg	agatctttct	480
aggaagatta	ttgtttanaa	ttatgaaagg	antagggcag	ggacagggcc	agaagtanaa	540
ganaacattg	cctatanccc	ttgtcttgca	cccagatgct	ggacaagggt	tca	593

<210> 217

<211> 335

<212> DNA

<213> Homo sapien

<400> 217

tgacaccttg	tccagcatct	gacgtgaaga	tgagcagctc	agaggaggtg	tcttggattt	60
cctggttctg	tggtgtccgt	ggcaatgaat	tcttctgtga	agtggatgaa	gactacatcc	120
aggacaaatt	taatcttact	ggactcaatg	agcaggtccc	tactatcga	caagctctag	180
acatgatctt	ggacctggag	cctgatgaag	aactggaaga	caaccccaac	cagagtgacc	240
tgattgagca	ggcagccgag	atgctttatg	gattgatcca	cgcccgtac	atccttacca	300
accgtggcat	cgccagatg	ctggacaagg	tgca			335

<210> 218

<211> 248

<212> DNA

<213> Homo sapien

<400> 218

tacgtactgg	tcttgaaggt	cttaggtaga	gaaaaaatgt	gaatatttaa	tcaaagacta	60
tgatgaaat	gggactgtaa	gtacagaggg	aagggtggcc	cttatcgcca	gaagttggta	120
gatgcgtccc	cgtcatgaaa	tggtgtgtca	ctgcccagca	tttgccgaat	tactgaaatt	180
ccgtagaatt	agtgcaaat	ctaactgtgt	tcatctaaga	ttatggttcc	atgtttctag	240
tactttta						248

<210> 219

<211> 530

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (530)

<223> n = A,T,C or G

<400> 219

tgacgcttgg	ccacttgaca	caagtagggg	ataaggacaa	agacccatna	ggtggcctgt	60
cagccttttg	ttactgttgc	ttccctgtca	ccacggcccc	ctctgtaggg	gtgtgctgtg	120
ctctgtggac	attggtgcat	tttcacacat	accattctct	ttctgcttca	cagcagtcct	180
gaggcgggag	cacacaggac	taccttgtca	gatgangata	atgatgtctg	gccaactcac	240
cccccaacct	tctcactagt	tatangaaga	gccangccta	naaccttcta	tctgncccc	300

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ttgccctatg acctcatccc tgttccatgc cctattctga tttctggtga actttggagc 360
agcctggttt ntccctctca ctccagcctc tctccatacc atggtanggg ggtgctgttc 420
cacncaaang gtcaggtgtg tctggggaat cctnananct gccnggagtt tccnangcat 480
tcttaaaaac cttcttgctt aatcanatng tgtccagtgg ccaacntcn 530

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<210> 220

<211> 531

<212> DNA

<213> Homo sapien

<400> 220

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tgacgcttgg ccacttgaca ctaaataagca tcttctaaag gcctgattca gagttgtgga 60
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ctgtgtttct gctggaaaag gaggaagag gaatggctga ttttaccta atgtctccca 180
gtttttcata ttctcttgg atctcttct ctgacaactg ttcccttttg gtctcttct 240
tcttgctcag agagcaggtc tctttaaacc tgagaaggga gaatgagcaa atgattaaag 300
aaaacacact tctgaggccc agagatcaaa tattaggtaa atactaaacc gcttgctgctc 360
tgtggtcact tttctctct ttcacatgct ctatccctct atccccacc tattcatatg 420
gcttttatct gccagttat ccggcctctc atcaaccttc tcccctagcc tactggggga 480
tatccatctg ggtctgtctc tgggtgtattg gtgtcaagtg gccaagcgtc a 531

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<210> 221

<211> 530

<212> DNA

<213> Homo sapien

<400> 221

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attgacgctt ggccacttga caccgcctg cctgcaatac tggggcaagg gccttcactg 60
ctttctgcc accagctgcc actgcacaca gagatcagaa atgctaccaa ccaagactgt 120
tggctctcag cctctctgag gagaaagag agaagcctgg aagtcagaag agaagctaga 180
tcggctacgg ccttggcagc cagcttcccc acctgtggga ataaagtctg gcattgctta 240
acaatggggg cacctctga gaaacacatt gttaggcaat tcggcgtgtg ttcacagag 300
catatttaca caaacctcga tagtgagcc tactatccac tattgctcct acgtgcaaa 360
cctgaacagc atgggactgt actgaatact ggaagcagct ggtgatggtg cttatttgtg 420
tatctaaaca cagagaagggt acagtaagaa tatggtatca taaacttaca gggaccgcca 480
tcctatatgc agtctgttgt gaccaaagtg tgtcaagtgg ccaagcgtca 530

```

<210> 222

<211> 578

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (578)

<223> n = A, T, C or G

<400> 222

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tgtatcgacg tagtggctct cgggctacta ggccgttgtg tgetggtagt acctggttca 60
ctgaaaggcg catctcctc cccgcgtcgc cctgaagcag ggggaggact tcgcccagcc 120
aaggcagttg tatgagtttt agetgaggca ctctgagacc tctgagccca cctccttcag 180
gagccttccc cgattaagga agccagggtg aggattcctt cctccccag acaccacgaa 240
caaaccacca cccccctat tctggcagcc catatacatc agaacgaaac aaaataaaca 300
aataaacnaa aaccaaaaaa aaaagagaag gggaaatgta tatgtctgtc catcctgttg 360
ctttagcctg tcagctccta nagggcaggg accgtgtctt ccgaatggtc tgtgcagcgc 420

```

cgactgcggg aagtatcgga ggaggaagca gaggcagcag aagttgaacg gtgggcccgg 480
 cggtctcttg gggctgggtg tgaacttoga gaccgctttc gctttttgtc ttagattttac 540
 gtttgcctct tggagtggga naccactacn tcnatata 578

<210> 223

<211> 578

<212> DNA

<213> Homo sapien

<400> 223

tgtatcgacg tagtgggtctc ctcttgcaaa ggactggctg gtgaatgggt tccctgaatt 60
 atggacttac cctaaacata tcttatcacc attaccagtt gcaaaatatt agaattgtgt 120
 gtcactgttt catttgattc ctagaagggt agtcttagat atgttacttt aacctgtatg 180
 ctgtagtgct ttgaatgcac tctttgtttg catttttgtt tgcccaacct gtcaattata 240
 gctgcttagg tctggactgt cctggataaa gctgttaaaa tattcaccag tccagccatc 300
 ttacaagcta attaatgcaa ctaaatgctt ccttggtttg ccagacttgt tatgtcaatc 360
 ctcaatttct ggggttcattt tgggtgccct aaatcttagg gtgtgacttt ctttagcatcc 420
 tgtaacatcc attcccaagc aagcacaact tcacataata ctttcagaa gttcattgct 480
 gaagcctttc cttcaccag cggagcaact tgattttcta caacttccct catcagagcc 540
 acaagagtat gggatatgga gaccactacg tcgatata 578

<210> 224

<211> 345

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) A (345)

<223> n = A, T, C or G

<400> 224

tgtatcgacg tantgggtctc ccaagggtgct gggattgcag gcatgagcca ccactcccag 60
 gtggatcttt ttctttatac ttaattcatt aggtttctgt tattcaagaa gtgtagtgggt 120
 aaaagtcttt tcaatctaca tgggttaaata atgatagcct gggaaataaa tagaaatttt 180
 ttctttcatc tttaggttga ataaagaaac agaaaaata gaacatactg aaaataatct 240
 aagttccaac catagaagaa ctgcagaaga aatgaagaaa gtgatgatga ttttagatttt 300
 gatattgatt tagaagacac aggaggagac cactacgtcg ataca 345

<210> 225

<211> 347

<212> DNA

<213> Homo sapien

<400> 225

tgtatcgacg tagtgggtctc caaactgagg tatgtgtgcc actagcacac aaagccttcc 60
 aacagggacg caggcacagg cagtttaaag ggaatctgtt tctaaattaa tttccacctt 120
 ctctaagtat tctttcctaa aactgatcaa ggtgtgaagc ctgtgctctt tcccaactcc 180
 cctttgacaa cagccttcaa ctaacacaag aaaaggcatg tctgacactc ttcttgagtc 240
 tgactctgat acgttggtct gatgtctaaa gagctccaga acaccaagg gacaattcag 300
 aatgctgggt tataacagac tccaatggag accactacgt cgatata 347

<210> 226

<211> 291

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(281)

<223> n = A,T,C or G

<400> 226

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aggngnggga ntgtatcgac gtagtgggtc cccaacagtc tgtcattcag tctgcagggtg      60
tcagtgtttt ggacaatgag gcaccattgt cacttattga ctctcagct ctaaagtctg      120
aaattaaatc ttgtcatgac aagtctggaa ttctgatga ggttttacaa agtatttttg      180
atcaatactc caacaaatca gaaagccaga aagaggatcc tttcaatatt gcagaaccac      240
gagtggattt acacacctca ggagaccact acgtcgatac a                                281

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<210> 227

<211> 3646

<212> DNA

<213> Homo sapien

<400> 227

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gggaaacact tctcccagc cttgtaaggg ttggagccct ctccagtata tgctgcagaa      60
tttttctctc ggttttctcag aggattatgg agtccgcctt aaaaaaggca agctctggac      120
actctgcaaa gtagaatggc caaagtttgg agttgagtgg ccccttgaag ggtcactgaa      180
cctcacaatt gttcaagctg tgtggcgggg ttgtaactgaa actcccgcc tccctgatca      240
gtttccctac attgatcaat ggctgagttt ggtcaggagc acccttccg tggctccact      300
catgcaccat tcataatttt acctccaagg tctcctgag ccagaccgtg ttttcgcctc      360
gacctcagc cggttcggct cgccctgtac tgccctctc tgaagaagag gagagtctcc      420
ctcaccagc cccaccgct taaaaccagc ctactccctt agggcatcc catgtctcct      480
cggctatgtc cctgtaggc tcatcaccca ttgctcttg gttgcaaccg tgggtggagg      540
aagtagccc tctactacca ctgagagagg cacaagtccc tctgggtgat gagtgtcca      600
cccccttct ggtttatgtc ccttctttct acttctgact tgtataattg gaaaaccat      660
aatctcctc tctctgaaaa gcccaggtt ttgacctac tgatggagtc tgtactctgg      720
acacattggc ccacctggga tgactgtcaa cagctccttt tgacctttt cacctctgaa      780
gagagggaaa gtatccaaag agaggccaaa aagtacaacc tcacatcaac caataggccg      840
gaggaggaag ctagaggaat agtgattaga gacccaattg ggacctaat gggacccaaa      900
tttctcaagt ggaggagaa cttttgacga tttccaccgg tatctcctcg tgggtattca      960
gggagctgct cagaaacct taaactgtc taaggcgact gaagtcgtcc aggggcatga      1020
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tgacctggca gcccgcgaaa atagccatgc tcttaatttg gcatttgtgg ctcaggcagc      1140
cccagatagt aaaaggaaa tccaaaaact agagggattt tgctggaatg aataccagtc      1200
agcttttaga gatagcctaa aagggttttg acagtcaaga ggttgaaaaa caaaaacaag      1260
cagctcaggc agctgaaaaa agccactgat aaagcatcct ggagtatcag agtttactgt      1320
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ctgactcaaa ctccactatt cctgttcacg actgtcagga actgttgga actactgaa      1440
ctggccgacc tgatcttcaa aatgtgccc taggaaagggt ggatgccacc atgttcacag      1500
acagtagcag cttctcagag aagggtact gaaaggccgg tcagctgtt accatggaga      1560
cagatgtgtt gtgggtcag gctttaccag caaacacctc agcacaaaag gctgaattga      1620
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ggtaaccaga aagctgattc agcagctcaa gatgcagtg gactttcagt cacgcctcta      1860
aacttgetgc ccacagtctc ctttccacag ccagatctgc ctgacaatcc cgcatactca      1920
acagaagaag aaaactggcc tcagaactca gagccaataa aaatcaggaa ggttggtgga      1980
ttcttctga ctctagaatc ttcatacccc gaactcttg gaaaacttta atcagtcacc      2040
tacagtctac caccatttta ggaggagcaa agctacctca gctcctccg agccgtttta      2100

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agatccccc	tcttcaaagc	ctaacagatc	aagcagctct	ccggtgcaca	acctgcgccc	2160
aggtaaagtc	caaaaaaggt	cctaaaccca	gcccaggcca	ccgtctccaa	gaaaactcac	2220
caggagaaaa	gtgggaaatt	gactttacag	aagtaaaacc	acaccgggct	gggtacaaat	2280
accttctagt	actggttagac	accttctctg	gatggactga	agcatttgct	accaaaaacg	2340
aaactgtcaa	tatggttagt	aagtttttac	tcaatgaaat	catccctcga	catgggctgc	2400
ctgtttgcca	tagggtctga	taatggaccg	gccttcgcct	tgtctatagt	ttagttagtc	2460
agtaaggcgt	taaacattca	atggaagctc	cattgtgcct	atcgacccca	gagctctggg	2520
caagtagaac	gcatagaactg	caccctaaaa	aacactctta	caaaattaat	cttagaaacc	2580
ggtgtaaatt	gtgtaagtct	ccttccttta	gccctactta	gagtaagggtg	cacccttac	2640
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aacagagccc	aactagaaac	atgggtcccc	agggtgggt	caggccccct	aaaactgcac	3060
ctaagttggg	tgaagccatt	agattaattc	tttttcttaa	ttttgtaaaa	caatgcatag	3120
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caatgatttg	attcccccaa	aaacacaagt	ggggaatgta	gtgtccaacc	tggtttttac	3240
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ggccctccac	cagcaaaaag	attctgactc	actgaagact	tggatgatca	ttagtatttt	3600
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<210> 228

<211> 419

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1)...(419)

<223> n = A,T,C or G

<400> 228

taagagggtg	caagatctaa	gcacagccgt	caatgcagaa	cacagaacgt	agcctggtaa	60
gtgtgttaag	agtggaatt	tttgagtag	agagtaaggc	acctaacct	agctggggtt	120
tggtagcgt	cccagatggc	ttacagaaga	aagtgtcctg	agatgagttt	ttaagaatga	180
ataaggatag	acacaagtga	ggactgactt	ggcagtggtg	aatggtgggt	ggcaaaaaac	240
ttcgcatgta	tggaaactgc	acgtacagga	atgaagaatg	agactgtgtg	gtgtttaatg	300
agctgcaaat	actaatttta	tcctgaaagt	tttgaagagt	taactaadaa	gtatttttta	360
gtaaggaaat	aacctacat	ttcagggtta	ttgtttgttt	andtattgaa	gggtcccaa	419

<210> 229

<211> 148

<212> DNA

<213> Homo sapien

<400> 229

aagagggtac	ctgtatgtag	ccatggtggc	aatgagagac	tgattactac	ctgctggaga	60
ttgtttaagt	gagttaatat	attaaggata	aaggagacca	ggttttttga	ctgttggaga	120
aggaaattac	agataatgaa	gggtcccaa				148

<210> 230
<211> 257
<212> DNA
<213> Homo sapien

<400> 230

taagagggtgta cmaaaaaaaaaaaa aaatagaac gaatgagtaa gacctactat ttgatagtac 60
aacagggtga ctatagtcaa tgataactta attatacatt taacatagag tgaattgga 120
ttgtttgtaa ctgaaggat aaatgcttga gaggatggat acceccattct ccatgatgta 180
cttatttcac attacatgcc tgtatcaaag catctcatat accctataaa tatgtacacc 240
tactatgtac cctctta 257

<210> 231
<211> 260
<212> DNA
<213> Homo sapien

<400> 231

taagagggtgta cgggtatttg ctgatgggat ttttttttct ttctttttct ttggaaaaca 60
aaatgaaagc cagaacaaaa ttattgaaca aaagacaggg actaaatctg gagaaatgaa 120
gtccctcac ctgactgcca tttcattcta tctgaccttc cagtctaggt taggagaata 180
gggggtggag gggattaatc tgatacaggt atatttaaag caactctgca tgtgtgccag 240
aagtccatgg taccctctta 260

<210> 232
<211> 596
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(596)
<223> n = A,T,C or G

<400> 232

tgctcctctt gccttaccac ccacaaatta gaaccataat gagatgtcac ctcataacctg 60
gtgggattaa cattatttaa aaaatcagaa gtattgacaa ggatgtgaag aaattagaac 120
atctgtgcac tgttggtggg aatgtaaaaa aggtgtggcc actatgggta acagcatgaa 180
ggttcctcaa aaaaaatttt ttttaattcta ctctatgac gatcttgagg ttgtttatgc 240
aaaagaactg aaatcaggat tttgaggaaa tattcacatt cccacatcca tttctgcttt 300
attcataata ctcaagagat ggaaacaacc taaatgtcca tcccgggatg aatggataaa 360
cacagtgtgg tatatgcata caatggaata ttatttagtc tttaaaaaga aaaattctat 420
catatactac aacttanatn aaccttgagg acacaatgct nagtgaaata agccacggaa 480
ggacgaatac tgcattattc ccttatatga agtatctaaa gtggtcaaac tcttanagca 540
naaagtaaaa atgggtgggt gccanacagt tggttaggcn agaaganaan cctant 596

<210> 233
<211> 96
<212> DNA
<213> Homo sapien

<400> 233

tcttctgaag acctttcgcg actcttaagc tctgtggttg taaggcaaga ggagcgttgg 60
taaggcaaga ggagcgttgg taaggcaaga ggagca 96

<210> 234
<211> 313
<212> DNA
<213> Homo sapien

<400> 234
tgtaagtcga gcagtgtgat gataaaactt gaatggatca atagttgctt cttatggatg 60
agcaaagaaa gtagtttctt gtgatggaat ctgctcctgg caaaaatgct gtgaacgttg 120
ttgaaaagac aacaaagagt tttagagtagt acataaattt agaatagtag ataaacttag 180
aatagtacat aaacttagta cataaataat gcacgaagca ggggcagggc ttgagagaaat 240
tgacttcaat ttggaagag tatctactgt aggttagatg ctctcaaaca gcacacact 300
gctcgactta caa 313

<210> 235
<211> 550
<212> DNA
<213> Homo sapien

<400> 235
aacgaggaga gatccttaaa aagaatgttg agtgaaaaaa gtagaaaata agataatctc 60
caaagtccag tagcattatt taaacatttt taaaaaatat actgataaaa attttgtaca 120
tttcccaaaa atacatatgg aagcacagca gcataaatgc ctatgggrtt gaggataggg 180
gttgggagta gggatgggga taaaggggga aaataaaacc agagaggagt cttacacatt 240
tcatgaacca aggagtataa ttatttcaac tatttgtacc wgaagtccag aaagagtgga 300
ggcagaaggg ggagaagagg gcgaagaac gtttttggga gaggggtccc asaagagaga 360
ttttcgcgat gtggcgctac atacgttttt ccaggatgcc ttaagctctg caccctattt 420
ttctcatcac taatattaga ttaaaccctt tgaagacagc gtctgtggtt tctctacttc 480
agctttccct ccgtgtcttg cacacagtag ctgttttaca agggttgaac tgactgaagt 540
gagattattc 550

<210> 236
<211> 325
<212> DNA
<213> Homo sapien

<400> 236
tagactgact catgtcccct accagagtag ctagaattaa tagcacaagc ctctacaccc 60
aggaactcac tattgaatac ataatggaa tttattcagc cttaaaaagt ttggaaggaa 120
attctgacat atgctaaaac atggatgaac cttgaagact ttatgataag taaaagaagc 180
cagtcataaa aggaaaaata ttgcatgatt ccacttatat gaggtaccta gagtagtcaa 240
tttcatagaa acacaaaata gaatgggtgt tgccagggct tttgaggaaa agggatgac 300
aagttagggg acatgagtca gtcta 325

<210> 237
<211> 373
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(373)
<223> n = A,T,C or G
<400> 237

tagactgact catgtcccct atctactcaa catttccact tgaagtctga taggcatctc 60
 agacttatct tgtcccaaag caaactcttt atttcttttc atcttagtct ttatttcttg 120
 tgctgtctta cccatctcaa aagagtgccaa aaatccacca agttgtctgaa acagaaatct 180
 aagaaatata cttgattctt ctttttccca tctacttcac ttctaattca ttagtaataa 240
 atctgtttca gaaaacaaa cacctcatgt tctactcat aagggggagt tgaacaatga 300
 gaacacacag acacagggag gggaacatca cacaccacgg cccgtcaggg agtangggac 360
 atgagtcagt cta 373

<210> 238

<211> 492

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(492)

<223> n = A,T,C or G

<400> 238

tagactgact catgtcccct ataatgtctc caggcatcag aaagcatctc aaactggagc 60
 tgacaccatg gcagagggtt caggtaagtc acaaaagggg tctaaagaa tttgccctca 120
 atatcagagt gattagaaga agtggacaga gctacccaag ttaacatat gcgagataaa 180
 aaaaatattg cacttgtgaa cacacactac aggaggaaaa taaggaacat aatagcatat 240
 tgtgtctata tgatgatgaa gaacctctct anaagaaaac ataaccaaa aaacaaagaa 300
 aattcctgcn aatgtttaat gctatagaag aaattaacaa aaacatatat tcaatgaatt 360
 cagaaaagtt agcagggtcan aagaaaacaa atcaaagacc agaataatcc cattttagat 420
 tgcgagtaa actanaacag aaagaatacc actggaaatt gaattcctac gtangggaca 480
 tgantcanc ta 492

<210> 239

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(482)

<223> n = A,T,C or G

<400> 239

tggaaagtat ttaatgatgg gcaacttgct gtttacttcc tacatatccc atcatcttct 60
 gtattttttt aaataacttt tttttggatt tttaaagtaa cttattctg agaggtaaca 120
 tggattacat acttctaagc cattaggaga ctctatgtta aaccaaagg aaatgttact 180
 agatcttcat ttgatcaata ggatgtgata atcatcatct ttctgtctta atggaaaagt 240
 actanaaaca tggaaaccata atcttagatg aacaacgtta gaatttgac taattctacg 300
 gaatttcagt aattcggcaa atgtcgggca gtgacacaac atttcatgac ggggacgcac 360
 ctaccaactt ctggcgataa gggccaccct tccctctgta cttacagtc catttcatac 420
 acagtctttg attaaatatt cacatttttt ctctacctaa agaccttcaa gaccagtacg 480
 ta 482

<210> 240

<211> 519

<212> DNA

<213> Homo sapien

<220>
<221> misc feature
<222> (1) ... (519)
<223> n = A,T,C or G
<400> 240
tgtatcgacg tagtgggtctc cccatgtgat agtctgaaat atagcctcat gggatgagag 60
gctgtgcccc agcccgacac ccgtaaagggt tctgtgctga ggtggattag taaaagagga 120
aagccttgca gttgagatag aggaagggca ctgtctcctg cctgccccctg ggaactgaat 180
gtctcggat aaaacccgat tgtacatttg ttcaattctg agataggaga aaaaccaccc 240
tatggcggga ggcgagacat gttggcagca atgctgcctt gttatgcttt actccacaga 300
tgtttgggcy gagggaaaca taaatctggc ctacgtgcac atccaggcat agtacctccc 360
tttgaactta attatgacac agattccttt gctcacatgt ttttttgctg accttctcct 420
tattatcacc ctgctctcct accgcattcc ttgtgctgag ataataaaaa taatatcaat 480
aaaaacttga nggaactcgg agaccactac gtcgataca 519

<210> 241

<211> 771

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1) ... (771)

<223> n = A,T,C or G

<400> 241

tgtatcgacg tagtgggtctc cactccccgc ttgacggggc tgctatctgc cttccaggcc 60
actgtcacgg ctccccggta gaagtcactt atgagacaca ccagtgtggc cttgttggct 120
tgaagctcct cagaggagggt tgggaacaga gtgaccgagg gggcagcctt gggctgacct 180
aggacggtca gcttgggtccc tccgccaaac acgagagtgc tgctgcttgt atatgagctg 240
cagtaataat cagcctcgtc ctacgcctgg agcccagaga tggtcaggga ggccgtgttg 300
ccanacttgg agccagagaa gcgattagaa acccctgagg gccgattacc gacctcataa 360
atcatgaatt tgggggcttt gcttgggtgc tgttggtacc angagacatt attataacca 420
ccaacgtcac tgctggttcc antgcaggga aaatggttga tcnnaactgtc caagaaaacc 480
actacgtcca taccatcca ctaattgcn gccgcctgca ggttcaacca tattggggaa 540
naactcccn ccgcggtttg ggattgncat naacctttga aatttttcc tattanttgt 600
ccccataaaa taaacnttg ggcnttaate cattgggtcc atancttnt tnccegggtt 660
ttaaanttg tttatccgc cncctnattt ccccccaac tttccaaaac ccgaaacnt 720
tnaaattnt tnaaacctg gggggttccc nnaattnnan ttnaancnc c 771

<210> 242

<211> 167

<212> DNA

<213> Homo sapien

<400> 242

tgggcacctt caatatcggg ctcatcgata acatcacgct gctgatgctg ctgttgctgg 60
tctctcttag gaacctctgg attttcaaat tctttgagga attcatcaa attatctgcc 120
tctctcctt tctctctttt tctaaggctt tctggtacaa gcggtca 167

<210> 243

<211> 338

<212> DNA

<213> Homo sapien

<400> 243

ttgggcacct	tcaatatcta	ctgatctaaa	tagtgtgggt	tgaggcctct	tggtcctggc	60
taaaaatcct	tggaagagt	caatctccac	tttacaatag	aggtaaaaat	cttacaatgg	120
atattcttga	caaagctagc	atagagacag	caattttaca	caaggatatt	ttcacctggt	180
taataacagt	ggttttccta	cacccatagg	gtgccacca	gggaggagt	cacagttgca	240
gaaacaaatt	aagatactga	agacaacact	acttaccatt	tcccgatatag	ctaaccacca	300
gttcaactgt	acatgtatgt	tcttatgggc	aatcaaga			338

<210> 244

<211> 346

<212> DNA

<213> Homo sapien

<400> 244

tttttggtc	ccatacagca	cactctcatg	ggaaatgtct	gttctaaggt	caaccataa	60
tgcaaaaatc	atcaatatac	ttgaagatcc	cctgtgaagg	tacaatgtat	ttaatattat	120
cactgataca	attgatccaa	taccagtttt	agtctggcat	tgaatcaaat	cactgttttt	180
gttgataaaa	aagagaaata	tttagcttat	atttaagtac	catattgtaa	gaaaaaagat	240
gcttatcttt	acatgctaaa	atcatgatct	gtacattggt	gcagtgaata	ttactgtaaa	300
aggaagaag	gaatgaagac	gagctaagga	tattgaaggt	gcccaa		346

<210> 245

<211> 521

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (521)

<223> n = A,T,C or G

<400> 245

accaatccca	cacggatact	gagggacaag	tatatcatcc	catttcatcc	ctacagcagc	60
aacttcatga	ggcaggaggt	attagtccca	ttttacagaa	gaggaaactg	agacttaggg	120
agatcaagta	atttggccag	gtcgacaaat	tagtgataga	gccagggtt	gaagcgacgt	180
ctgtcttaag	ccaatgaccc	ctgcagatta	ttagagcaac	tggtctccac	aacagtgtaa	240
gcctcttget	anaagctcag	gtccacaagg	gcagagattt	ttgtctgttt	tgctcattgc	300
tccttcccca	ttgcttagag	cagggctctgc	cacgaancag	gttctcaatg	catagttatt	360
aaatgtatat	aagagcaaac	atatgttaca	gagaactttc	tgtatgcttg	tcacttacat	420
gaatcacctg	tganatgggt	atgcttggtc	cccantgttg	cagatnaaga	tattgaangt	480
gcccaaatca	ctanttgagg	gcgcctgcan	gtccancata	t		521

<210> 246

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (482)

<223> n = A,T,C or G

<400> 246

tggaaccaat	ccaatatccc	atcaatgata	gactggataa	agaaaatttg	gcacatgttc	60
------------	------------	------------	------------	------------	------------	----

accatgaaat actatgcagc cataaaaaag gatgagttca taccctttgc agggacatgg 120
atgaagctgg agaccatcat tctcagcaaa ctaacaaggg aacagaaaac caaacactgc 180
atgttctcac tcttaagtgg gagctgaaca atgagaacac atggacacag ggagggggaac 240
atcacacagt ggggcctgct ggtgggtagg ggtctagggg agggatagca ttaggagaaa 300
tacctaattg agatgacggg ttgatgggtg cagcaaacca ccatgacacg tgtataccta 360
tgtaacaaac ctgcatgttc tgcacatgta cccagaact taaagtgtta ataaaaaaat 420
taagaaaaaa gttaagtatg tcatagatac ataaaatatt ghanatattg aagggtgcccc 480
aa 482

<210> 247

<211> 474

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1) ... (474)

<223> n = A, T, C or G

<400> 247

ttcgatacag gcacagagta agcagaaaaa tggctgtggt ttaaccaagt gagtacagtt 60
aagtgagaga ggggcagaga agacaagggc atatgcaggg ggtgattata acagggtggtt 120
gtgctgggaa gtgagggtac tcggggatga ggaacagtga aaaagtggca aaaagtggta 180
agatcagtga attgtacttc tccagaattt gatttctggn ggagtcaa atactatccag 240
tttgggggat catanggcaa cagttgaggt ataggaggtga gaagtcncag tgggataatt 300
gaggttatga anggtttggt actgactggt actgacaang tctgggttat gaccatggga 360
atgaatgact gtanaagcgt anaggatgaa actattccac ganaaagggg tccnaaaact 420
aaaaannnaa gnnnnngggg aatattattt atgtggatat tgaangtgcc caaa 474

<210> 248

<211> 355

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1) ... (355)

<223> n = A, T, C or G

<400> 248

ttcgatacag gcaaacatga actgcaggag ggtgggtgacg atcatgatgt tgccgatggt 60
ccggatggnc acgaagacgc actgganac gtgcttacgt ccttttctc tgttgatggc 120
cctgagggga cgcaggaccc ttatgacctc cagaatcttc acaacgggag atggcactgg 180
attgantccc antgacacca gagacacccc aaccaccagn atatcantat attgatgtag 240
ttcctgtaga nggccccctt gtggaggaaa gctccatnag ttggtcatct tcaacaggat 300
ctcaacagtt tccgatggct gtgatgggca tagtcatant taacntgtgn tcgaa 355

<210> 249

<211> 434

<212> DNA

<213> Homo sapien

<400> 249

ttggattggt cctccaggag aacaagggga aaaagggtgac cgagggctcc ctggaactca 60
aggatctcca gyagcaaaaag gggatggggg aattcctggt cctgctggtc ccttaggtcc 120

```

acctggctct ccaggcttac caggctctca aggcccaaag ggtaacaaag gctctactgg 180
acccgctggc cagaaagggt acagtgggtc tccagggcct cctgggcctc caggctccacc 240
tggatgaagtc attcagcctt taccaatctt gtctccaaa aaaacgagaa gacatactga 300
aggcatgcaa gcagatgcag atgataatat tcttgattac tcggatggaa tggagaagaat 360
atttgggtcc ctcaattccc tgaaacaaga catcgagcat atgaaatttc caatgggtac 420
tcagaccaat ccaa 434

```

<210> 250

<211> 430

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (430)

<223> n = A,T,C or G

<400> 250

```

tggattggtc acatggcaga gacaggattc caaggcagtg agaggaggat acaatgcttc 60
tcactagtta ttattattta ttttattttt gagatgaagt ctgcctttgt ctcccaggct 120
ggagagcggg ggtgcgatct tggctctctg caacccccgc ctcaagcaat tctcctgtct 180
tagcctcgcg ggtagatgga attacaggcg cccaccgccca tgcccaacta atttttttgt 240
gtcttcagta gagacagggg ttgccatgt tgggcaggct ggtcttgaac tctgacctc 300
nagtgatctg cctcctcgg cctcacaag tgctggaatt acaggcatgg gctgctgcac 360
ccagtcaact tctcactagt tatggcctta tcattttcac cacattctat tggcccaaaa 420
aaaaaaaaan 430

```

<210> 251

<211> 329

<212> DNA

<213> Homo sapien

<400> 251

```

tggctactcca ccatyatggg gtcaaccgcc atcctcgccc tctcctcggc tgttctccaa 60
ggagtctgtg ccgagggtgca gctggtgcag tctggagcag aggtgaaaaa gtccggggag 120
tctctgaaga tctcctgtaa gggttctgga tacaccttta agatctactg gatcgctcgg 180
gtgcgccagt tgcccgggaa aggcctggag tggatggggc tcatctttcc tgatgactct 240
gataccagat acagcccgtc cttccaaggc caggtcacca tctcagtcga taagtccatc 300
agcaccgcct atctgcagtg gagtaccaa 329

```

<210> 252

<211> 536

<212> DNA

<213> Homo sapien

<400> 252

```

tggctactcca ctccagccaa ccttaattaa gaattaagag ggaacctatt actattctcc 60
caggctcttc tgccttaacc aggtctctgg gacagtatta gaaaaggatg tctcaacaag 120
tatgtagatc ctgtactggc ctaagaagtt aaactgagaa tagcataaat cagaccaaac 180
ttaatggctg ttgagacttg tgcctcggag cagctgggat aggaaaactt ttgggcagca 240
agaggaagaa ctgcctggaa gggggcatca tgttaaaaat tacaagggga acccacacca 300
ggcccccttc ccagctctca gcctagagta ttagcatttc tcagctagag actcacaact 360
tctttgctta gaatgtgcca ccggggggag tccctgtggg tgatgaggct ctcaagagtg 420
agagtggcat cctatcttct gtgtgccac aggagcctgg cccgagactt agcaggtgaa 480
gtttctggtc caggctttgc ccttgactca ctatgtgacc tctggtggag taccaa 536

```

<210> 253

<211> 507

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (507)

<223> n = A,T,C or G

<400> 253

```

ntgttgcatg cccagtaact cggaagctg aggcgggagg atcacctgag ctgaggaggt      60
tgaggccgca gtgagccggg accacgccac tacactccag cctggggcat agagtggagac      120
cctccaagac agaaaagaaa agaaaaggaa ggaaagggaa agggaaaagg aaaaggaaaa      180
ggaaaaggaa aaggaaaaga caagacaaaa caagacttga atttgatct cctgacttca      240
attttatgtt cttttacac cacaattcct ctgcttacta agatgataat ttagaaaccc      300
ctcgttccat tctttacagc aagctggaag tttggtcaag taattacaat aatagtaaca      360
aatttgaata ttatatgcca ggtgttttct attcctgctc tcaactaatt ctcaccactc      420
tgatataaat acaattgctg cggggtgtgg tggctcatgc ctgtaatccc ggcactttgg      480
gagaccgagg tgggaggats gcaacaa                                     507

```

<210> 254

<211> 222

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (222)

<223> n = A,T,C or G

<400> 254

```

ttggattggt cactgtgagg aagccaaatc ggatccgaga gtctttttct aaaggccagt      60
actggccaca ctttctcctg ccgccttcct caaagctgaa gacacacaga gcaaggcgct      120
tctgttttac tccccaatgg taactccaaa ccatagatgg ttagctnccc tgctcatctt      180
tccacatccc tgctattcag tatagtcctg ggaccaatcc aa                                     222

```

<210> 255

<211> 463

<212> DNA

<213> Homo sapien

<400> 255

```

tgttgcatgc cataaatgct gaaatggaaa taaacaacat gatgaggagg gattaagttg      60
gggaggggagc acattaaggt ggccatgaag tttgttggaa gaagtgactt ttgaacaagg      120
ccttggtgtt aagagctgat gagagtgtcc cagacagagg ggccactggt acaatagacg      180
agatgggaga gggcttggaa ggtgtgcgaa ataggaagga gtttgttctg gtatgagtct      240
agtgaacaca gaggcgagag gccctggtgg gtgcagctgg agagttatgc agaataacat      300
taggcctgtg gggggactgt agactgtcag caataatcca cagtttggat tttattctaa      360
gagtgatggg aagcctgtya aaggggggta agcaaggagt gaaattatca gatttacagt      420
gataaaaaata aattggtctg gctactgggg aaaaaaaaaa aaa                                     463

```

<210> 256

<211> 262

<212> DNA

<213> Homo sapien

<400> 256

```
ttggattggt caactgctc aactctacyt ttctctcttc ttcttaaaaa attaatgaat      60
ccaatacatt aatgccaaaa ccttggggtt ttatcaatat ttctgtttaa aagtattatc      120
cagaactgga cataatacta cataataata cataacaacc ccttcactctg gatgcaaaca      180
tctattaata tagcttaaga tcactttcac ttacagaag caacatcctg ttgatgttat      240
tttgatgttt ggaccaatcc aa                                         262
```

<210> 257

<211> 461

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(461)

<223> n = A,T,C or G

<400> 257

```
gnggnnnnnn nnncaattcg actcngttcc cntgggtancc ggtcgacatg gccgcgggat      60
taccgcttgt nntcgggggt gtatggggga ctatgaccgc ttgtagctgg ggggtgatgg      120
gggactatga ccgcttgtag mtggkggtgt atgggggact atgaccgctt gtcgggtggt      180
cggataaacc gacgcaaggg acgtgatcga agctgcgttc ccgctcttcc gcacgcgtag      240
ggatcatgga cagcaatatc cgcattcgyc tgaaggcgtt cgaccatcgc gtgctcgatc      300
aggcgaccgg cgacatcgcc gacaccgcac gccgtaccgg cgcgctcatc cgcgggtccga      360
tcccgttcc caccgcgcatc gagaagttca cgggtcaaccg tggcccgcac gtcgacaaga      420
agtcgcgcga gcagttcgag gtgcgtacct acaagcggtc a                                         461
```

<210> 258

<211> 332

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(332)

<223> n = A,T,C or G

<400> 258

```
tgaccgcttg tagctggggg tgtatggggg actacgaccg cttgtagctg ggggtgtatg      60
ggggactatg accgcttgta gctgggggtg tatgggggac tatgaccgct tgtagctggg      120
ggtgtatggg ggactaggac cgcttgtagc tgggggtgta tgggggacta tgaccgcttg      180
tagctggggg tgtatggggg actacgaccg cttgtagctg ggggtgtatg ggggactatg      240
accgcttgta nctgggggtg tatgggggac tatgaccgct tgtgctgcct gggggatggg      300
aggagagttg tgggtgggga aaaaaaaaaa aa                                         332
```

<210> 259

<211> 291

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (291)

<223> n = A, T, C or G

<400> 259

taccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt	60
gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt	120
gaccgcttgt gaccgcttgt nacnggggggt gtctggggga ctatgannga ntgtnactgg	180
gggtgtctgg gggncatga nngantgtna cnggggggtgt ctgggggact atganngact	240
gtgcnnccctg ggggatcnga ggagantngn ggtagnat ggtngggan a	291

<210> 260

<211> 238

<212> DNA

<213> Homo sapien

<400> 260

taagagggta ctggttaaaa tacaggaaat ctggggtaat gaggcagaga accaggatac	60
tttgaggtca gggatgaaaa ctagaatttt tttctttttt tttgcctgag aaacttgctg	120
ctctgaagag gcccatgtat taattgcttt gatcttcctt ttcttacagc cctttcaagg	180
gcagagccct ccttatcctg aaggaatctt atccttagct atagtatgta ccctctta	238

<210> 261

<211> 746

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (746)

<223> n = A, T, C or G

<400> 261

ttgggcacct tcaatatcaa tagctaacaat ttattgagtgt tttatcgtat cataaaacac	60
tggttctaagc ctttaaactgt actaattcat ttaatgctca taatcacttt agaagggtggg	120
tactagtatt agtctcattt acagatgcaa catgcaggca cagagagggt aattaacttg	180
cccaaggtaa cacagctaag aatagaaaa aatattgaat ctggaaagtt gggcttctgg	240
gtaaccaca gagtcttcaa tgagcctggg gctcactca gtttgctttt acaaagcgaa	300
tgagtaacat cacttaattc agtgagtagg ccaaatggag gtcagctacg agtttctgct	360
gttcttgagc tggactgaca gatgtttaca acgtctggcc atcagtwaat ggactgatta	420
tcattgggaw gtgggtgggc tgaatgttgg ccagtgaagt ttattcawgc catattttta	480
tgtttaggat gacttttggc tggctctagg gcaagctctg tctgscacgg aacacagaat	540
wacacagga cccctcaat ttctgggtgt gctagaacca tgaaccactg gttgggggaa	600
caagcggta aaacctaat gggccgggt ggcagggtcc acccatatgg ggaaaactcc	660
cnacgcgtt ggaatgcctn agctngaatt attctaanag ttgtccnct aaaattagcc	720
tgggcgttaa tcanggtcn naagcc	746

<210> 262

<211> 588

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (588)

<223> n = A, T, C or G

<400> 262
tgaccgcttg tcatctcaca tggggtcctg cacgcttttg cctttgtagg aaacctgaca 60
tttgtctgtt tcttctttct cttttccttc ccatatcctc ctaatttacg tttgacttgt 120
ttgctgagga ggcaggagct agagactgct gtgagctcat aggggtggga agtttatcct 180
tcaagtcccg cccactcacc actgcttctc accttccctt gaccaggctt acaagtgggt 240
tcttgctgc tttccctttg gacccaacaa gccctgttaa tgagtgtgca tgactctgac 300
agctgtggac tcagggtcct tggctacagc tgccatgtaa aatatctcat ccagttctcg 360
caaattgtta aaataaccac atttcttaga ttccagtacc caaatcatgt ctttacgaac 420
tgctcctcac acccagaagt ggcacaataa ttcttgggga attattactt ttttttttct 480
ctctnttnc gnnngnnnng gnnngnccag gaattaccac nttggaagac ctggccngaa 540
tttattatan aggggagcgg attntttttc ctaacacaaa gcggttca 588

<210> 263

<211> 730

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (730)

<223> n = A,T,C or G

<400> 263

tttttttttt tttggcctga gcaactgaaa ttatgaaatt tccatatact caaaagagta 60
agactgcaaa aagattaaat gtaaaagttg tcttgataac agtaatgttt aagataccta 120
ttanatttat aaatggaaaa ttagggcatt tggatataca agttgaaaat tcaggagtga 180
ggttgggctg gctgggtata tactgaaaac tgtcagtaca cagatgacat ctaaaaccac 240
aaatctgggt ttatttttagc agtgatatgt gtcactccca caaaagcctt cccaattggc 300
ctcagcatac acaacaagtc acctcccccac agccctctac acataaacia attccttagt 360
ttagttcagg aggaaatgcg cccttttctt tccgctctag gtgaccgcaa ggcccagttc 420
tcgtcaccaa gatgttaagg gaagtctgcc aaagaggcat ctgaaaggaa ataaggggaa 480
tgggagtgc cacaaggaa agccaaggan aaactttgga gaccgtttct aganccttg 540
catttcacaa caaaactcng gaacaaacct tgtctcatca atcatttaag cccttcgttt 600
ggannagact ttctgaactg ggcgtgaac ataancctca ttgaatgtct tcacagtctc 660
ccagctgaag gcacaccttg ggccagaagg ggaatcttcc aggtcctcaa nacagggttc 720
gccctttgnc 730

<210> 264

<211> 715

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (715)

<223> n = A,T,C or G

<400> 264

tttttttttt tttggccagt atgatagtct ctaccactat attgaagctc ttaggtcatt 60
tacacttaat gtggttatag atgctgttga gcttacttct accaccttgc tatttctccc 120
gtctcttttt tgttcttttt ctcttctttt cctcccttat tttataattg aatttttttag 180
gattctattt tatatagatt tatcagctat aacactttgt attcttttgt tttgtgggtc 240
ttctgtcatt tcaatgtgca tcttaaacct atcacaatct attttcaa ataatcatat 300
aaccttacat ataatgtaag aatctaccac catatatttc catttctccc ttccatccta 360

tgtntgtcat atttttttct ttatatatgt tttaaagaca taatagtata tgggaggttt 420
ttgcttaaaa tgtgatcaat attccttcaa ngaaacgtaa aaattcaaaa taaatntctg 480
tttattctca aatnnaccta atatttctta ccatntctna tacntttcaa gaatctgaag 540
gcattgggtt ttccgggtt aagaacctcc tctaaagcac tctaagcaga attaagtctt 600
ctgggagagg aattctccca agcttggggc ttannntgta ctccntnang gttaaanttt 660
ggccgggaaa tagaaattcc aagttaacag gntanttttt ntntntntn tcncc 715

<210> 265

<211> 152

<212> DNA

<213> Homo sapien

<400> 265

tttttttttt tttcccaaca caaagcacca ttatctttcc tcacaatttt caacatagtt 60
tgattcccat gaagaggtta tgatttctaa agaaaacatg gctactatac tatcaatcag 120
ggttaaactc tttttttttg agacggagtt ta 152

<210> 266

<211> 193

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) (193)

<223> n = A,T,C or G

<400> 266

taaactcgt ccttcttta atcaatatgg aggtaccaca ctccacatta ccttcttttc 60
aagggaactt ttccgttaact gttgtgggta ttacagacca ggcttctaaa cctcttaaaa 120
ctccccaatt ctggtgccaa ctgggacaac atgctttttt tttttttttt tttttttttt 180
gagacggagt tta 193

<210> 267

<211> 460

<212> DNA

<213> Homo sapien

<400> 267

tgttgcgatc ccttaagcat ggggtgctatt aaaaaaatgg tggagaagaa aatacctgga 60
atttacgtct tatctttaga gattgggaag accctgatgg aggacgtgga gaacagcttc 120
ttcttgaatg tcaattccca agtaacaaca gtgtgtcagg cacttgctaa ggatcctaaa 180
ttgcagcaag gctacaatgc tatgggattc tcccaggagg gccaatctct gagggcagtg 240
gctcagagat gcccttcacc tcccatgatc aatctgatct cgggtggggg acaacatcaa 300
ggtgtttttg gactccctcg atgccagga gagagctctc acatctgtga cttcatccga 360
aaaacactga atgctggggc gtactccaaa gttgttcagg aacgcctcgt gcaagccgaa 420
tactggcatg acccataaaa ggaggatgtg gatcgcaaca 460

<210> 268

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (533)

<223> n = A,T,C or G

<400> 268

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tgttgcgatc cgttgataga atagcgacgt ggtaatgagt gcatggcacy cctccgactt 60
accttcgccc gtggggaccc cgagtagctc tacggcgctc tcacttagag taccctctgg 120
acgcccgggc gcgttcgatt taccggaagc gcgagctgca gtgggcttgc gccccggcc 180
aaattctttg gggggtttaa ggccggggg aatttgaggt atctctatca gtagtagcc 240
aagttggaac agtcgccatt cccgaaatcg ctttctttga atccgcaccg cctccagcat 300
tgctcattc atcaacctga aggcacgcat aagtgaagggt tgtgtcttca gtagctccac 360
tccataacta gcgcgtcga cctcgtcttc gtagcgcca ggtccgtgcy tgcgaattcc 420
caactccggt gagttgcga tttcaagttt cgaaactggt cgctccacn atttggcatg 480
ttcacgcatg acacggaata aactcgcca gtaccgggaa tgggacgca aca 533

```

<210> 269

<211> 50

<212> DNA

<213> Homo sapien

<400> 269

```

tttttttttt ttgcctgaa ttagctacag atctctctca caagcgggtca 50

```

<210> 270

<211> 519

<212> DNA

<213> Homo sapien

<400> 270

```

tgttgcgatc caaataaccc accagcttct tgcacacttc gcagaagcca cagtcctttg 60
gctgagtcac gtgaacggtc agtgcaagca gccgcgtgcc agagcagagg tgcagcatgc 120
tgcacaccag ctcagggtcg acctcctcca gcaggatgga caggatggag tgcagcatgc 180
tgtccaccac ctcctggcac tcttccgaca gggacttcgg cagcttcgag acattttgt 240
caaaagcgtc gagtatttct ttctcagctc tgttgtgtgc 300
tcaccaggaa ttccacaccc tcacagaaa catcaga 360
taatggggtc caccagttcc agggcagggg tgaca 420
ccagagtctg catgggcac tctttcacct catcacagaa cccaaccagc gcaatctct 480
ccttgggttg catgtgcac atcatctggg atcgcaaca 519

```

<210> 271

<211> 457

<212> DNA

<213> Homo sapien

<400> 271

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tttttttttt ttccggcggc gaccggacgt gcactcctcc agtagcggct gcacgtcgtg 60
ccaatggccc gctatgagga ggtgagcgtg tccggcttcg aggagttcca ccgggcgctg 120
gaacagcaca atggcaagac cattttcgcc tactttacgg gttctaagga cgcggggggg 180
aaaagctggt gccccgactg cgtgcaggct gaaccagtcg tacgagaggg gctgaagcac 240
attagtgaag gatgtgtgtt catctactgc caagtaggag aagagcctta ttggaaagat 300
ccaataatg acttcagaaa aaacttgaaa gtaacagcag tgcctacact acttaagtat 360
ggaacacctc aaaaactggt agaactctgag tgtcttcagg ccaacctggt ggaaatgttg 420
ttctctgaag attaagattt taggatggca atcaaga 457

```

<210> 272

<211> 102

<212> DNA

<213> Homo sapien

<400> 272

tttttttttt ttgggcaaca acctgaatac attttcaagg ctctggcttg ggtcaagcc 60
cgcaggggaa atgcaactgg ccaggteaca gggcaatcaa ga 102

<210> 273

<211> 455

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (455)

<223> n = A,T,C or G

<400> 273

tttttttttt ttggcaatca acagggttaa gtcttcggcc gaagttaatc tctgttttt 60
ggcaatcaac aggtttaagt ctccggccga agttaatctc gtgttttttg caatcaacag 120
gtttaagtct tccggcgaag ttaatctctg gtttttggca atcaacaggt ttaagtcttc 180
ggccgaagtt aatctctgtt ttttgcaat caacaggttt aagtcttcgg ccgaagttaa 240
tctctgtttt ttggcaatca acagggttaa gtcttcggcc gaagttaatc tctgttttt 300
ggcaatcaag aggtttaagt ctccggccga agttaatctc gtgttttttg caatcaacag 360
gtttaagtct tccggcgaan ttaatctctg gtttttggca atcaacaggt ttaagtcttc 420
ggccgaagtt aatctctgtt ttttgcaat caana 455

<210> 274

<211> 461

<212> DNA

<213> Homo sapien

<400> 274

tttttttttt ttggccaata cccttgatga atcatcaatgt gaaaatectc ggtaaaatac 60
tggaacagc cctccaaag caatcaaaa agcttatcca catgatcaa gtgggetttc 120
tccctgggga caaggtctgg ttcaacataa gaaaatcaat aaatgtaatc catcacataa 180
acagaaccaa agacaaaaac cacatgatta tctcaataga tgcagaaaag gccttgga 240
aattcaacag cccttcattg taaacactct taataaacta gatattgatg gaatgtatct 300
caaaataata agagctatgt atgacaaacc cacagccaat atcactactga atgggcaaag 360
actggaagca tcccttttga aaactggcac aagacaagga tgccctctct caccgctcct 420
attcaacata gtattggaag ttctggccag ggcaatcaag a 461

<210> 275

<211> 729

<212> DNA

<213> Homo sapien

<220>

<221> misc_features

<222> (1)... (729)

<223> n = A,T,C or G

<400> 275

tttttttttt ttggccaaca ccaagtcttc cagtgaggag gttttattat gttttacaac 60
catgaaaaca taggaaggtg gctgttacag caaacatttc agatagacga atcggccaag 120

```

ctccccaac cccaccttca cagcctcttc cacacgtctc ccanagattg ttgtccttca 180
cttgcaaatt canggatgtt ggaagtngac atttnnagtn gcnggaaccc catcagtga 240
ncantaagca gaantacgat gactttgana nacanctgat gaagaacacn ctacnganaa 300
ccctttctnt cgtgttanga tctcngtcc ntcactaatg cggccccctg cnggtccacc 360
atttgggaga actccccccn cgttggtacc ccccttgagt ntcccattct ngccccccan 420
accngncttg ngngncantn cncctcnca ccntgtttcc ctgngngtnaa aatnngtttt 480
nccgccnccc naattccac ccnaatcaca gcgaancng aaggccttcn naagtgttta 540
angeccngng gtttctctnt ntanttgag cctaccctcc cncctnnmnt tncnggttgg 600
tcgcgcctg gncncgctn gttcctcttt nnggnnaca cctngntcnn nggncntcn 660
nnctnttcc tnnnactagc tngcctntcc ncnccngngn ncanngcaca ttncnccnac 720
tntgtnncc 729

```

<210> 276

<211> 339

<212> DNA

<213> Homo sapien

<400> 276

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tgacctgaca ttagtagat acttaataaa ttttgtgga atgaatggat gaagtggagt 60
tacagagaaa aatagaaaag tacaaattgt tgcagtgtt ttgaaggaaa attatgatct 120
ttcccaaagt tctgacttca ttctaagaca gggttagtag cccatacat aattttactt 180
gcttttgaaa atcaaatgag ataattctatt tagattgata atttatttag actggctata 240
aactattaag tctagcaaa tatacatttt aattctattt tccacctctt gtgatatagc 300
tatgtagggt ttgactttaa tggatgtcag gtcaatccc 339

```

<210> 277

<211> 664

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (664)

<223> n = A,T,C or G

<400> 277

```

tgacctgaca tccataacaa aatctttctc cattatatto ttctagggga atttcttgaa 60
aagcatccaa aggaaacaaa tgatggtaag accgtgccaa gtggggagca gacaccaaag 120
taagaccaca gattttacat tcaacaggta gctcacagta ctttgcccga cactgtgggc 180
agaaatagcc tctaattgta agcctggct cagtattgcc atccaaatgc gccatgctga 240
aagagggttt tgcactctgg tcagatnaag aagcaatggg gtgctgagga aatcccatc 300
gaataagtga gcattcagaa cttgagctag caggaggagg actaagatga tgtgtgagca 360
actctttgta atggctttca tctaaaataa catggtacgt gccaccagtt tcacgagcaa 420
gtacagtgca aacgcgaact tctgcagaca atccaataac agatactcta attttagctg 480
cctttagggt cttgattaaa tcataaatat tagatggatc gcaagttgta agyngtctaa 540
aagatgatta gtacttctcg acttgatgt ccaggcatgt tgttttaaan tctgccttag 600
nccctgctta ggggaatttt taaagaagat ggctctccat gttcanggtc aatcacnaat 660
tgcc 664

```

<210> 278

<211> 452

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) .. (452)

<223> n = A,T,C or G

<400> 278

```

tgacctgaca ttgaggaaga gcacacacct ctgaaattcc ttaggttcag aagggcattt    60
gacacagagt gggcctctga taattcatga aatgcattct gaagtcaccc agaattggagg    120
ctgcaatctg ctgtgctttg ggggttgctt cactgtgctc ctggatatca cacaaaagct    180
gcaatccttc ttcttcaact aacattttgc agtattttgt gggattttta ctgcagacat    240
gatacatagc ccatagtgcc cagagctgaa cctctggttg agagaagttg ccaaggagcg    300
ggaaaaatgt cttgaaagat ctataggcca ccaatgctgt catcttaciaa cttgaacttg    360
gccattctg tatggttgca tgcagatctt ggagaagagt acgcctctgg aagtcacggg    420
atatccaan ctgtctgtca gatgtcaggt ca                                     452

```

<210> 279

<211> 274

<212> DNA

<213> Homo sapien

<400> 279

```

tttttttttt ttgggcaagg caaatttact tctgcaaaag ggtgctgctt gcacttttgg    60
ccactgagag agcacaccaa acaaagtagg gaaggggttt ttatccctaa cgcggttatt    120
ccctggttct gtgtcgtgtc cccattgggt ggagtcagac tgcacaatct acactgaccc    180
aactggctac tgtttaaaat tgaatatgaa taattaggta ggaaggggga ggctgtttgt    240
tacgttaciaa gacgtgtttg ggcattgtcag gtca                                     274

```

<210> 280

<211> 272

<212> DNA

<213> Homo sapien

<400> 280

```

tacctgacat ggagaaataa cttgtagtat tttgcgtgca atggaatact atatgagggt    60
gaaaatgaat gaactagcaa tgcgtgtatc aacatgaata aatcccaaaa acataataat    120
gttgaatgga aaaggtgagt ttcagaagga tatatatgcc ctctaaatcc atttatgtaa    180
acctttaaaa aactacatta tttatggcca taagtcacac cagaaaatat ttaaaaacct    240
acatgggatt gataactact gatgtcaggt ca                                     272

```

<210> 281

<211> 431

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) .. (431)

<223> n = A,T,C or G

<400> 281

```

tttttttttt ttggccaata gcatgattta aacattggaa aaagtcaaag gagcaatgag    60
aattttttatg ttctcttgaa taatcaaaag agtaggcaac attggttcct cattcttgaa    120
tagcattaat cagaaaatat tgcatagcct ctagcctcct tagagtaggt gtgctctctc    180
aaatatatca tagtcccaca gtttatttca tgtatatatt ctgcttgaat cacatagaca    240
tttgaatttg caacgcctga tgtaaataa taaattctta ccaatcagaa acatagcaag    300
aaattcaggg acttggtcat yatcagggta tgacagcana tcctgtara aacactgata    360

```

cacactcaca cacgtatgca acgtggagat gtcgcyttww kkktywccwm rmrycrwecn 420
aatcacttan n 431

<210> 282
<211> 98
<212> DNA
<213> Homo sapien

<400> 282
attcgattcg atgcttgagc ccaggagttc aagactgcag tgagccactg cacttcaggc 60
tggaacaacag agcgagtcce tgtgccaaaa aaaaaaaaaa 98

<210> 283
<211> 764
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (764)
<223> n = A, T, C or G

<400> 283
tttttttttt ttgcgaagca cgtgcacttt attgaatgac actgtagaca ggtgtgtggg 60
tataaactgc tgtatctagg ggcaggacca agggggcagg ggcaacagcc ccagcgtgca 120
gggccascac tgcacagtgg astgcaaagg ttgcaggcta tggggcgcta ctavtaaccc 180
cgtttttctt gtattatctg taacataata tggtagactg tcacagagcc gaatwccart 240
hacagatga atccaawggt caygaggatg cccasaatca gggcccasat sttcaggcac 300
ttggcggtgg gggcatasgc ctgkgccccc gtcacgtcsc caaccwtcty cctgtcccta 360
cmcttgawtc cncnccttnn nntnccntna tntgcccgcc cncctectng ngtaaacng 420
natctgcaat anctccctcn ccccttntgg antctcttcc ttcaantaan nttatccttn 480
acncccccct cncctttccc ctncncncn tnatccngn ncnctatca ntentnccct 540
cncntnctn cnatcggtc cncctnntaa ctacncttn ncnannct cactnatncc 600
ngnnantttt ttcccttccc ccnaccgcn tgcgtgcgc cgtctngcct nnnctnccna 660
cccnactttt atttaccttt ncaccctagc nctctacttn acccancnc tectacctcc 720
ngnccacccc nncctnate nctnnetctn tcnctcntt cccc 764

<210> 284
<211> 157
<212> DNA
<213> Homo sapien

<400> 284
caagtgtagg cacagtgatg aaagcctgga gcaaacacaa tctgtgggta attaacgttt 60
atttctcccc ttccaggaac gtcttgcatg gatgatcaaa gatcagctcc tggtaacat 120
aaataagcta gtttaagata cgttccccta cacttga 157

<210> 285
<211> 150
<212> DNA
<213> Homo sapien

<400> 285
attcgattgt actcagacaa caatatgcta agtggagaa gtcagtcaca aaagaccaca 60
tactgtatga cttcatttac attaagtgtc cagaatagga aaatccgtag agacagaaag 120

tagatgagca gctgcctagg tctgagtaca 150

<210> 286
<211> 219
<212> DNA
<213> Homo sapien

<400> 286

attcgatttt tttttttttg gccatgatga aattcttact ccttcagatt ttttgtctgg 60
ataaatgcaa gtctcaccac cagatgtgaa attacagtaa accttgaagg aatctcctga 120
gcaaccttgg ttaggatcaa tccaatatc accatctggg aagtcaggat ggctgagttg 180
caggtcttta caagttcggg ctggattggt ctgagtaca 219

<210> 287
<211> 196
<212> DNA
<213> Homo sapien

<400> 287

attcgattct tgaggctacc aggagctagg agaagaggca tggaaacaaat tttccctcat 60
atccatactc agaaggaacc aaccctgctg acaccttaat ttcagcttct ggctctaga 120
actgtgagag agtacatttc tcttggttta agccaagaga atctgtcttt tggacttta 180
tatcatagcc tcaaga 196

<210> 288
<211> 199
<212> DNA
<213> Homo sapien

<400> 288

attcgatttc agtccagtc cagaacccac attgtcaatt actactctgt araagattca 60
tttgttgaaa ttcatagagt aaaacattta tgatccctta atatatgcca attaccatgc 120
taggtactga agattcaagt gaccgagatg ctagcccttg ggttcaagt atccctctcc 180
cagagtgcac tggactgaa 199

<210> 289
<211> 182
<212> DNA
<213> Homo sapien

<400> 289

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<210> 290
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<212> DNA
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<400> 290

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<210> 291

<211> 1851

<212> DNA

<213> Homo sapien

<400> 291

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<210> 292

<211> 1851

<212> DNA

<213> Homo sapien

<400> 292

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<210> 293

<211> 668

<212> DNA

<213> Homo sapien

<400> 293

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<210> 294

<211> 1512

<212> DNA

<213> Homo sapien

<400> 294

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<210> 295

<211> 1853

<212> DNA

<213> Homo sapien

<400> 295

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<210> 297

<211> 1855

<212> DNA

<213> Homo sapien

<220>

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<400> 297

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attaatggc aaagcactgc tcttatacgg tctgatatc gaatcaaaaa acaaggataa 1380
gatctactaa ttttatcttc aaaatactga aatgcattca ttttaacatt gacgtgtgta 1440
agggccagtc ttccgtattt ggaagctcaa gcataactg aatgaaaata ttttgaaatg 1500
acctaattat ctaagacttt atttttaata ttgttatttt caaagaagca ttagagggta 1560
cagttttttt tttttaaatg cacttctggg aaatactttt gttgaaaaca ctgaatttgt 1620

aaaaggtaaat acttactatt ttccaatttt tccctcctag gatttttttc cccaatgaa 1680
tgtaagatgg caaaatttgc cctgaaatag gttttacatg aaaactccaa gaaaagttaa 1740
acatgtttca gtgaatagag atcctgctcc ttgggcaagt tctaaaaaa cagtaataga 1800
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<210> 298

<211> 1059

<212> DNA

<213> Homo sapien

<400> 298

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gcgcttgrgg agactmcgat gacagygcct tcatggagcc caggtaccac gtccgtggag 180
aagatctgga caagctccac agagctgccc tgggtgggta aagtccccag aaaggatctc 240
atcgtcatgc tcagggacac tgaygtgaac aagarggaca agcaaaagag gactgctcta 300
catctggcct ctgccaatgg gaattcagaa gtagtaaac tctgtctgga cagacgatgt 360
caacttaatg tcttgacaa caaaaagagg acagctctga yaaaggccgt acaatgccag 420
gaagatgaat gtgcgttaat gttgctggaa catggcactg atccaaatat tccagatgag 480
tatggaaata ccactctrca ctaygctrtc tayaatgaag ataaattaat ggccaaagca 540
ctgctcttat ayggtgctga tatcgaatca aaaaacaagg tatagatcta ctaattttat 600
cttcaaaata ctgaaatgca ttcattttta cattgacgtg tgtaagggcc agtcttccgt 660
atttggaagc tcaagcataa cttgaatgaa aatattttga aatgacctaa ttatctaaga 720
ctttatttta aatattgtta ttttcaaaga agcattagag ggtacagttt ttttttttta 780
aatgcacttc tggtaaatac ttttgttgaa aacactgaat ttgtaaaagg taatacttac 840
tatttttcaa tttttccctc ctaggatttt ttteccctaa tgaatgtaag atggcaaaat 900
ttgccctgaa ataggtttta catgaaaact ccaagaaaag ttaaaccatgt ttcagtgaat 960
agagatcctg ctcttttggc aagttcctaa aaaacagtaa tagatacgag gtgatggccc 1020
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<210> 299

<211> 329

<212> PRT

<213> Homo sapien

<400> 299

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Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu
20 25 30
Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
35 40 45
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
50 55 60
Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65 70 75 80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
85 90 95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
100 105 110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
115 120 125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
130 135 140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser

145 150 155 160
 Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
 165 170 175
 Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
 180 185 190
 Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
 195 200 205
 Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
 210 215 220
 Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
 225 230 235 240
 Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
 245 250 255
 Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
 260 265 270
 Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
 275 280 285
 Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
 290 295 300
 Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
 305 310 315 320
 Ser Met Leu Phe Leu Val Ile Ile Met
 325
 <210> 300
 <211> 148
 <212> PRT
 <213> Homo sapien
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 <400> 300
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 20 25 30
 Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
 35 40 45
 Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
 50 55 60
 Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
 65 70 75 80
 Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
 85 90 95
 Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
 100 105 110
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
 115 120 125
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser
 130 135 140
 Lys Asn Lys Val
 145

<210> 301

<211> 1155

<212> DNA

<213> Homo sapien

<400> 301

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agcaacgtgg	gcacttctgg	agaccacgac	gactctgcta	tgaagacact	caggagcaag	180
atgggcaagt	gggtgccgcca	ctgcttcccc	tgctgcaggg	ggagtggcaa	gagcaacgtg	240
ggcgcttctg	gagaccacga	cgactctgct	atgaagacac	tcaggaacaa	gatgggcaag	300
tggtgctgcc	actgcttccc	ctgctgcagg	gggagcggca	agagcaaggt	ggcgcttgg	360
ggagactacg	atgacagtgc	cttcatggag	cccaggtacc	acgtccgtgg	agaagatctg	420
gacaagctcc	acagagctgc	ctgggtgggt	aaagtcccca	gaaaggatct	catcgtcatg	480
ctcagggaca	ctgacgtgaa	caagaaggac	aagcaaaaga	ggactgctct	acatctggcc	540
tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcca	ggaagatgaa	660
tgtgcgttaa	tggtgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgctat	ctataatgaa	gataaattaa	tggccaaagc	actgctctta	780
tatggtgctg	atatcgaatc	aaaaaacaag	catggcctca	caccactgtt	acttgggtgta	840
catgagcaaa	aacagcaagt	cgtgaaattt	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
ctggatagat	atggaaggac	tgctctcata	cttgctgtat	gttgtggatc	agcaagtata	960
gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggacagacg	1020
gccagagagt	atgctgtttc	tagtcatcat	catgtaattt	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaaa	tgtctcaaga	1140
accagaaata	aataa					1155

<210> 302

<211> 2000

<212> DNA

<213> Homo sapien

<400> 302

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agcaacgtgg	gcacttctgg	agaccacgac	gactctgcta	tgaagacact	caggagcaag	180
atgggcaagt	gggtgccgcca	ctgcttcccc	tgctgcaggg	ggagtggcaa	gagcaacgtg	240
ggcgcttctg	gagaccacga	cgactctgct	atgaagacac	tcaggaacaa	gatgggcaag	300
tggtgctgcc	actgcttccc	ctgctgcagg	gggagcggca	agagcaaggt	ggcgcttgg	360
ggagactacg	atgacagtgc	cttcatggag	cccaggtacc	acgtccgtgg	agaagatctg	420
gacaagctcc	acagagctgc	ctgggtgggt	aaagtcccca	gaaaggatct	catcgtcatg	480
ctcagggaca	ctgacgtgaa	caagaaggac	aagcaaaaga	ggactgctct	acatctggcc	540
tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcca	ggaagatgaa	660
tgtgcgttaa	tggtgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgctat	ctataatgaa	gataaattaa	tggccaaagc	actgctctta	780
tatggtgctg	atatcgaatc	aaaaaacaag	catggcctca	caccactgtt	acttgggtgta	840
catgagcaaa	aacagcaagt	cgtgaaattt	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
ctggatagat	atggaaggac	tgctctcata	cttgctgtat	gttgtggatc	agcaagtata	960
gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggacagacg	1020
gccagagagt	atgctgtttc	tagtcatcat	catgtaattt	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaca	agacttaaag	1140
ctgacatcag	aggaagagtc	acaaagggtc	aaaggcagtg	aaaatagcca	gccagagaaa	1200
atgtctcaag	aaccagaaat	aaataaggat	ggtgatagag	aggttgaaga	agaaatgaag	1260

aagcatgaaa	gtaataatgt	gggattacta	gaaaacctga	ctaattggtgt	cactgctggc	1320
aatggtgata	atggattaat	tcctcaaagg	aagagcagaa	cacctgaaaa	tcagcaattt	1380
cctgacaacg	aaagtgaaga	gtatcacaga	atttgcgaa	tagtttctga	ctacaaagaa	1440
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tcagaggaag	agtcacaaag	gcttgagggc	agtgaaaatg	gccagccaga	gctagaaaat	1560
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attctgattc	atgaagaaaa	gcagatagaa	gtggttgaaa	aaatgaattc	tgagctttct	1860
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<210> 303

<211> 2040

<212> DNA

<213> Homo sapien

<400> 303

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agcaacgtgg	gcacttctgg	agaccacgac	gactctgcta	tgaagacact	caggagcaag	180
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ggcgcttctg	gagaccacga	cgactctgct	atgaagacac	tcaggaacaa	gatgggcaag	300
tggtgctgcc	actgcttccc	ctgctgcagg	gggagcggca	agagcaagg	gggcgcttgg	360
ggagactacg	atgacagtgc	cttcatggag	cccagggtacc	acgtccgtgg	agaagatctg	420
gacaagctcc	acagagctgc	ctggtgggg	aaagtcccca	gaaaggatct	catcgctcatg	480
ctcagggaca	ctgacgtgaa	caagaaggac	aagcaaaaaga	ggactgctct	acatctggcn	540
tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcc	ggaagatgaa	660
tgtgcgttaa	tggtgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgetat	ctataatgaa	gataaattaa	tggecaaaagc	actgctctta	780
tatggtgctg	atatcgaatc	aaaaaacaag	catggcctca	caccactggt	acttgggtgta	840
catgagcaaa	aacagcaagt	cgtgaaattt	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
ctggatagat	atggaaggac	tgctctcata	cttgcgtgat	gttgtggatc	agcaagtata	960
gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggaacagacg	1020
gccagagagt	atgctgtttc	tagtcatcat	catgtaattt	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaca	agacttaaaag	1140
ctgacatcag	aggaagagtc	acaaagggtc	aaaggcagtg	aaaatagcca	gccagagaaa	1200
atgtctcaag	aaccagaaat	aaataaggat	ggtgatagag	aggttgaaga	agaaatgaag	1260
aagcatgaaa	gtaataatgt	gggattacta	gaaaacctga	ctaattggtgt	cactgctggc	1320
aatggtgata	atggattaat	tcctcaaagg	aagagcagaa	cacctgaaaa	tcagcaattt	1380
cctgacaacg	aaagtgaaga	gtatcacaga	atttgcgaa	tagtttctga	ctacaaagaa	1440
aaacagatgc	caaaatactc	ttctgaaaac	agcaaccag	aacaagactt	aaagctgaca	1500
tcagaggaag	agtcacaaag	gcttgagggc	agtgaaaatg	gccagccaga	gaaaagatct	1560
caagaaccag	aaataataaa	ggatggtgat	agagagctag	aaaattttat	ggctatcgaa	1620
gaaatgaaga	agcacggaag	tactcatgtc	ggattcccag	aaaacctgac	taatggtgcc	1680
actgctggca	atggtgatga	tggaattaat	cctccaagga	agagcagaac	acctgaaagc	1740
cagcaatttc	ctgacactga	gaatgaagag	tatcacagtg	acgaacaaaa	tgatactcag	1800
aagcaatttt	gtgaagaaca	gaacactgga	atattacagc	atgagattct	gattcatgaa	1860
gaaaagcaga	tagaagtgg	tgaaaaaatg	aattctgagc	tttctcttag	ttgtaagaaa	1920
gaaaagaca	tcttgcatga	aaatagtagc	ttgcgggaag	aaattgccat	gctaagactg	1980
gagctagaca	caatgaaaca	tcagagccag	ctaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	2040

<210> 304
<211> 384
<212> PRT
<213> Homo sapien
<400> 304
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20 25 30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
35 40 45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
50 55 60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65 70 75 80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
85 90 95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
100 105 110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
115 120 125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
130 135 140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145 150 155 160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
165 170 175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
180 185 190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
195 200 205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
210 215 220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225 230 235 240
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
245 250 255
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
260 265 270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
275 280 285
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
290 295 300
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
305 310 315 320
Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
325 330 335
Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val
340 345 350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
355 360 365
Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys
370 375 380

<210> 305

<211> 656

<212> PRT

<213> Homo sapien

<400> 305

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
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 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys

385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
 435 440 445
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
 450 455 460
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
 465 470 475 480
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
 485 490 495
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
 500 505 510
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
 515 520 525
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
 530 535 540
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
 545 550 555 560
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
 565 570 575
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
 580 585 590
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
 595 600 605
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
 610 615 620
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
 625 630 635 640
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
 645 650 655

<210> 306

<211> 671

<212> PRT

<213> Homo sapien

<400> 306

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
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 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe

115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
 385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
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Application for a Patent in the Field of



INVENTOR

DATE

BY

ATTORNEY

FILED

THE INVENTION OF THE ABOVE-NAMED INVENTOR IS SET FORTH IN THE FOLLOWING CLAIMS:

CLAIMS

1. A method of...

2. A method of...

3. A method of...

4. A method of...

THIS PAGE BLANK (USPTO)

5. A method of...

6. A method of...

7. A method of...

8. A method of...

9. A method of...

10. A method of...

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
19 October 2000 (19.10.2000)

PCT

(10) International Publication Number
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(51) International Patent Classification⁷: C12N 15/12, C07K 14/47, 16/18, 19/00, C12N 15/62, A61K 38/17, 39/395, 48/00, C12N 5/08, G01N 33/574, C12Q 1/68

(74) Agents: POTTER, Jane, E., R.; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 et al. (US).

(21) International Application Number: PCT/US00/09312

(22) International Filing Date: 7 April 2000 (07.04.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
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09/429,755 28 October 1999 (28.10.1999) US
09/534,825 23 March 2000 (23.03.2000) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).

Published:

— With international search report.

(72) Inventors: FRUDAKIS, Tony, N.; 7937 Broadmoor Pines Boulevard, Sarasota, FL 34243 (US). SMITH, John, M.; 208 - 116th Place S.E., Everett, WA 98208 (US). REED, Steven, G.; 2843 - 122nd Place N.E., Bellevue, WA 98005 (US). MISHER, Lynda, E.; 6251 53rd Avenue N.E., Seattle, WA 98115 (US). RETTER, Marc, W.; 33402 N.E. 43rd Place, Carnation, WA 98014 (US). DILLON, Davin, C.; 21607 N.E. 24th Street, Redmond, WA 98053 (US).

(88) Date of publication of the international search report:
28 June 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER



cDNA PREPARED FROM
NORMAL BREAST TISSUE
FROM THE SAME PATIENT

cDNA PREPARED
FROM BREAST TUMOR

818Aq1

(57) Abstract: Compositions and methods for the detection and therapy of breast cancer are disclosed. The compounds provided include nucleotide sequences that are preferentially expressed in breast tumor tissue, as well as polypeptides encoded by such nucleotide sequences. Vaccines and pharmaceutical compositions comprising such compounds are also provided and may be used, for example, for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of antibodies, which are useful for diagnosing and monitoring the progression of breast cancer in a patient.

WO 00/61753 A3

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C07K16/18 C07K19/00 C12N15/62
 A61K38/17 A61K39/395 A61K48/00 C12N5/08 G01N33/574
 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 45328 A (CORIXA CORPORATION) 15 October 1998 (1998-10-15) page 2, line 7 -page 5, line 22 page 7, line 23 -page 24, line 11; examples 1-4 sequence listing SEQ ID NOs:1, 3-10, 227	1,2,4-60
X	WO 97 25426 A (CORIXA CORPORATION) 17 July 1997 (1997-07-17) page 2, line 8 -page 5, line 11 page 7, line 14 -page 23, line 2; example 1 sequence listing SEQ ID NO:1, 3-10, 227 --- -/--	1,2,4-60

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

8 August 2000

Date of mailing of the international search report

08.11.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

MONTERO LOPEZ B.

INTERNATIONAL SEARCH REPORT

SI 000100

Int. Application No

PCT/US 00/09312

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO-97 25431 A (CORIXA CORPORATION) 17 July 1997 (1997-07-17) page 2, line 3 -page 3, line 25 page 4, line 12 -page 17, line 18; examples 1-4 sequence listing SEQ ID NOs:1, 3-10</p>	1,2,4-10

INTERNATIONAL SEARCH REPORT

international application No.
PCT/US 88/09312

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 21, 22, 29-31 34 37-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims N s.:

Claims 1, 2, 4-60 Partially.

Remark on Protest

- ☐ Th additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Partially 1, 2, 4-60

Breast cancer related polypeptide B18Ag1, corresponding polynucleotides comprising SEQ ID NOs:1, 3-10, or 227, and derived oligonucleotides; variants thereof, expression vector and host cell comprising the same; antibody and diagnostic kit containing it, fusion protein comprising the polypeptide; pharmaceutical composition and vaccine comprising any of the above and use therefor in the treatment of cancer, and for removing tumor cells from a sample; use of the polypeptides for stimulating and expanding T-cells and use of such T-cells for inhibiting cancer development; use of the polypeptides for determining the presence of cancer or monitoring the progression of cancer in a patient.

2. Claims: Partially 1-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B21GT2 (B311D) comprising SEQ ID NOs:56, 307, 308, 316 or 317.

3. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B15Ag1 comprising SEQ ID NOs:27 or 290.

4. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B31GA1b comprising SEQ ID NOs:148.

5. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B38GA2a comprising SEQ ID NOs:157.

6. Claims: Partially 1-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B11Ag1 (B305D) and its isoform A comprising SEQ ID NO:292-306, or 309-315.

**7. Claims: Claims: Partially 1, 2, 4-60,
all as far as applicable**

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Breast cancer related polypeptides, corresponding polynucleotides comprising SEQ ID NOs:11-26 (inventions 7-22), 28-55 (inventions 23-50), 57-86 (inventions 51-80), 142-147 (inventions 81-86), 149-156 (inventions 87-94), 158-226 (inventions 95-163), 228-253 (inventions 164-189), or 255-291 (inventions 190-226), and derived oligonucleotides; variants thereof, expression vector and host cell comprising the same; antibody and diagnostic kit containing it, fusion protein comprising the polypeptide; pharmaceutical composition and vaccine comprising any of the above and use therefor in the treatment of cancer, and for removing tumor cells from a sample; use of the polypeptides for stimulating and expanding T-cells and use of such T-cells for inhibiting cancer development; use of the polypeptides for inhibiting or monitoring the progression of cancer in a patient, as far as applicable.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No

PCT/US 00/09312

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9845328 A	15-10-1998	AU 6956098 A	30-10-1998
		EP 0975666 A	02-02-2000
		NO 994932 A	07-12-1999
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